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**Studies in Therapeutic
Arteriovenous Fistulae**

By

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CONTENTS

INTRODUCTION	5
REVIEW OF THE LITERATURE	6
CLINICAL MATERIAL	11
Construction of arteriovenous fistulae according to Cimino-Brescia	11
Results	17
ANGIOGRAPHIC STUDIES IN PATIENTS WITH CIMINO-BRESCIA ARTERIO- VENOUS FISTULAE (Together with J. Kaude)	23
HAEMODYNAMIC STUDIES IN PATIENTS WITH CIMINO-BRESCIA ARTERIOVENOUS FISTULAE (Together with I. Nordenfelt)	33
ADDUCTOR POLLICIS MUSCLE BLOOD FLOW IN PATIENTS WITH CIMINO- BRESCIA ARTERIOVENOUS FISTULAE	39
OTHER POSSIBLE COMPLICATIONS TO CIMINO-BRESCIA ARTERIO- VENOUS FISTULAE	43
On "hypertrophy" of the limb carrying the fistula	43
Morphological changes of the vessels involved septicaemia	43
Septicaemia	44
GENERAL DISCUSSION	45
CONCLUSIONS	51
SUMMARY	53
REFERENCES	55



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INTRODUCTION

Arteriovenous fistulae have been constructed surgically for various therapeutic purposes. Thus in young patients arteriovenous fistulae have been utilized with some success to promote skeletal growth of a shortened leg after poliomyelitis (Meyer et al. 1963, Vesely & Mears 1964). Less convincing therapeutic effects have been achieved when the fistulae have been used in an attempt to improve local circulation in extremities with gangrene (Roussiel 1919) and to increase blood supply to the brain in patients with various kinds of diminished cerebral blood flow (Hammer et al. 1950). Blaisdell et al. (1966) and Kistner & Vermeulen (1970) made arteriovenous fistulae distal to an arterial reconstruction; the increased blood flow was alleged to aid in keeping the reconstructed artery open.

In recent years therapeutic arteriovenous fistulae have been a valuable requisite for haemodialysis in acute and chronic renal failure. The technical resources for haemodialysis were available as early as in the late forties (Kolff et al. 1944, Alwall 1947) but the necessity for cut-down on the artery and vein for each dialysis and ligation of the vessels afterwards limited the use of haemodialysis to short-time treatment in acute renal failure. Alwall et al. (1949) reported attempts to construct permanent extracorporeal arteriovenous shunts, but the shunts clotted if they were not heparinized. It was not until 1960 that Quinton, Dillard & Scribner constructed functioning arteriovenous shunts using Teflon and Silastic, and thus made long-term haemodialysis treatment possible. The external shunts, however, gave complications with bleeding, thrombosis, infection etc. Many of these disadvantages might be overcome by the use of subcutaneous arteriovenous

fistulae as described by Brescia, Cimino, Appel & Hurwich (1966), often called Cimino-Brescia fistulae. These fistulae permitted dialysis after cannulation of the arterialized vein and have been used in many dialysis centers in all parts of the world (Ackman et al. 1967; Collste et al. 1967; Hanson et al. 1967; Klinkmann et al. 1967; Menno et al. 1967; Sperling et al. 1967; Suc et al. 1967; Verberckmoes et al. 1967; Röhl et al. 1968; Salomon et al. 1968; Skov & Fjeldborg 1968; Vellar et al. 1969; Lindstedt 1970).

Besides for haemodialysis Quinton-Scribner shunts have been used for repeated transfusions by Anderson et al. (1967), and for extracorporeal irradiation in leucemic patients (Chanana et al. 1968). Use of Cimino-Brescia fistulae for long-time intravenous therapy was described by Lindstedt, Lindergård & Nilsén (1967).

Cimino-Brescia arteriovenous fistulae have been used at this hospital for haemodialysis and for intravenous therapy since February 1967. From the beginning it was apparent that wide-spread clinical use of these fistulae would be facilitated by a knowledge of their local and general haemodynamic consequences (Lindstedt et al. 1967). The present work is a description of our experiences with Cimino-Brescia fistulae including a note on the surgical technique and the practical use of the enlarged veins. In addition studies of angiographic changes and local as well as general haemodynamic effects of the fistula will be given. Most of these studies were performed in 1967–69 at a time when it was not known if creation of an arteriovenous fistula entailed risks of circulatory complications, e.g. in elderly patients.

REVIEW OF THE LITERATURE

The literature about arteriovenous fistulae is voluminous and difficult to survey, for references see Callander (1920) and Holman (1937, 1962).

William Hunter (1757) is generally regarded as being the first to give a conclusive report on a case of acquired arteriovenous fistula diagnosed in vivo: it occurred at the elbow region after venesection. He also described many of the important pathological changes caused by the fistula, dilatation of the vein and artery, presence of a palpable thrill and a murmur. In 1833 Breschet reported several cases of acquired arteriovenous fistula. He described in detail the murmur typical for arteriovenous fistula and compared it to the sound from a spinning wheel or the sough from the bellows of a blacksmith.

Nicoladoni (1875) described slowing of the pulse rate after compression of the artery proximal to an arteriovenous fistula and the same was reported by Branham (1890). The phenomenon is most often called Branham's sign. Reid (1920, 1925) made experimental and clinical studies on arteriovenous fistulae and he and Callander (1920) reported a large series of patients mainly from Halsted's clinic. In very comprehensive and accurate experimental and clinical investigations Holman (1924–1963) studied the local and general effects of arteriovenous fistulae and our present knowledge of the consequences of an arteriovenous fistula is mostly founded on his work.

In Scandinavia Ingebrigtsen et al. (1960, 1963, 1965) made interesting studies of the blood flow and the morphological changes of the vessels close to the fistula.

Etiology of arteriovenous fistulae

Arteriovenous fistulae may be congenital or acquired. Congenital fistulae arise due to a defect in the development of the primitive vascular system. When the arteries and veins develop from the undifferentiated capillary plexus, the intermediate capillaries may be absorbed in some places and direct arteriovenous communication occurs. There is no clear demarcation between the congenital defects of haemangioma simplex, angioma teleangiectaticum, haemangioma cavernosum, strawberry birth mark, naevus angiectoides, port-wine mark, angioma arteriale rac-

mosum, cirroid aneurysm, serpentine aneurysm, congenital arteriovenous aneurysm, congenital arteriovenous fistula, Parks-Weber syndrome and Klippel-Trenaunay syndrome. The various types of fistula may occur in different parts of the body in the same patient. Fistulae are often multiple and it may be difficult to localize and to treat them. There is a strong tendency for these to increase in size in course of time and trauma may in some cases open up small communications so starting their growth.

Acquired arteriovenous fistulae are most often traumatic, but infections can also cause vascular lesions and rupture of an artery into a neighbouring vein. These are seen most often where artery and vein lie close together as in the extremities or in the neck. More centrally located fistulae seldom develop as death will usually occur due to bleeding into the body cavity or into the venous system. The history is most often of a penetrating wound with little external bleeding and the formation of a haematoma of moderate size. The typical signs of arteriovenous fistula, localized thrill, increased temperature, dilated, tortuous and sometimes pulsating veins and a typical continuous murmur may develop early or during the course of many years. There can be a direct communication between the artery and the vein, an aneurysmal varix (Hunter 1757), or an intermediate sac. The distinction between these types is of little clinical importance.

Most traumatic arteriovenous fistulae occurred during the wars and the pattern of their development has changed considerably with the advance of military technique. Few fistulae were caused by penetrating wounds from pointed weapons, but the development of small calibre rifles and grenades producing multiple small wounds, during World War I and especially World War II caused a considerable increase in the frequency of arteriovenous fistulae. With the alteration in the principles of treatment of vascular injuries during the Korean War and still more in the Vietnam conflict the relative frequency of arteriovenous fistulae has decreased.

In civilian life some arteriovenous fistulae are caused by surgical trauma. In early days this was mostly

venesection (Hunter 1757; Cooper 1836). Typical causes are mass-ligature of artery and vein e.g. during nephrectomy (Ekeström et al. 1968), percutaneous kidney biopsy (Boijesen & Köhler 1962, Ekelund & Lindholm 1971), operation for disc hernia (Areskog et al. 1964).

Haemodynamic effects of arteriovenous fistulae

"Flowing blood, like flowing water, has an inherent and natural tendency to follow the path of least resistance" (Holman). This principle determines the haemodynamic effects of an arteriovenous fistula.

Local flow patterns around an arteriovenous fistula are illustrated by Figures 1–3. Fig. 1 shows a small fistula where the opening is smaller than the diameter of the feeding artery. The blood from the central artery flows partly through the fistula and partly past the fistula into the artery distal to it. In the proximal venous limb the flow is centripetal whilst in the distal vein the flow may be in a central direction or be blocked by a valve held closed by increased venous pressure just distal to the fistula.

In a large acute fistula (Fig. 2) most of the blood flow from the central artery goes through the fistula. In the distal arterial limb the flow can continue in its normal direction towards the periphery but, in many larger fistulae is retrograde towards the fistula.

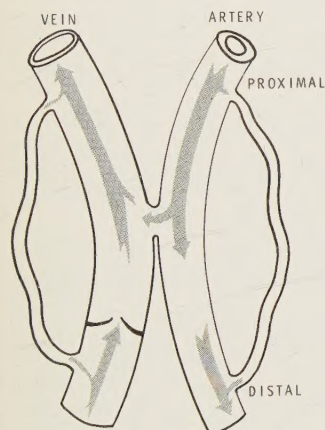
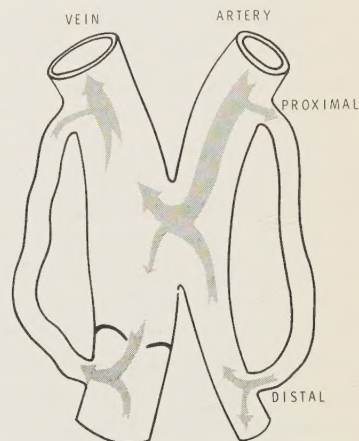


Fig. 1. BLOOD FLOW IN SMALL ACUTE ARTERIOVENOUS FISTULA. Flow is centrifugal in both proximal and distal artery, centripetal in both distal and proximal vein.

Fig. 2. BLOOD FLOW IN LARGE ACUTE ARTERIOVENOUS FISTULA. Flow through the fistula is larger. Blood flow in the distal artery may be centrifugal or centripetal, in the distal vein flow is often blocked by competent venous valve.



On the venous side the flow is directed centrally in the proximal vein. In the distal vein the flow is most often blocked by the venous valve.

With time the flow in the feeding artery to a large arteriovenous fistula (Fig. 3) increases and all blood from this artery may flow through the fistula. In the distal artery the flow can be retrograde.

An arteriovenous fistula is also a most efficient stimulus for the development of arterial collaterals and part of the blood from the collaterals flows to the fistula via the distal artery (Reid 1925). In the proximal vein the blood is, as usual, directed centrally. In the distal vein, if patent, the flow is directed peripherally as the valves have in most cases been destroyed by the high venous pressure.

General circulatory effects. Numerous studies of the haemodynamic effects of arteriovenous fistulae have been made in patients, and after the introduction of improved vascular suture technique by Carrel in 1902, large series of animal experiments have also been done. When an arteriovenous fistula is constructed, part of the cardiac output is short-circuited into the vein and returned to the right side of the heart. There are two parallel circuits competing for the blood, one through the fistula and one through the normal capillary bed. The flow in each circuit is in

Fig. 3. BLOOD FLOW IN LARGE CHRONIC ARTERIOVENOUS FISTULA. In the distal artery flow has become centripetal towards the fistula and collaterals fill the distal artery. In the vein distal to the fistula the valve has become incompetent, the flow is reversed to be directed centrifugally and blood returns towards the heart via distal collateral veins. The proximal artery has become wider and the wall is thinner.

principle inversely proportional to its resistance. Immediately after the opening of a large central arteriovenous fistula such as between the aorta and the inferior vena cava in the dog, systemic blood pressure falls, heart rate increases, the sizes of the heart and central blood vessels become smaller and this may occur within 24–28 hours (Holman 1962). In small fistulae permitting survival of the animal, the decreased systolic pressure gradually becomes normalized, but the diastolic pressure is permanently lowered. The pulse rate and the size of the heart return to normal and at the same time the circulating blood volume is increased. In long-standing fistulae the relation between the fistula and capillary flows tends to be stabilized in relation to the peripheral resistance in the fistula circuit. If the fistula is large, and the tissues around the artery and vein allow dilation of the vessels the equilibrium is never complete — the fistula flow increases steadily for many years. The blood vessels dilate from the fistula region up to the heart. The patient may develop dilation also of the heart and at last cardiac decompensation (Vollmar 1964). A vicious circle develops in these cases, the increased flow gives dilatation of the vessels and the dilatation of the vessels decreases the resistance and increases the fistula flow (Holman 1962).

The haemodynamic effects are related to the size and localization of the fistula and to the length of time which the fistula has been present. Holman (1924) reviewed the literature and his own clinical cases and found no sign of haemodynamic changes in fistulae smaller than 4 mm diameter, no matter how long the fistula had been present. Fistulae situated more centrally have a greater effect upon the heart than more peripheral fistulae (Holman 1940). Schumacker & Stahl (1949) found the enlargement of the heart to be more pronounced in fistulae localized in the lower half of the body than in the upper half. The enlargement of the heart generally disappears after surgical closure of the fistula.

Nicoladoni (1875) and later Branham (1890) noticed that the pulse rate decreased when an arteriovenous fistula was compressed. This is thought to be an effect caused by the increase in diastolic blood pressure due to an increase in peripheral resistance. This "Branham's sign" is regarded as a vagus reflex, as it can be inhibited by the administration of atropine. Branham's sign is not found in cases of small fistulae but it

has been found in some cases where an increase in the diastolic pressure could not be measured.

When an arteriovenous fistula is opened there is an immediate increase in cardiac output. Frank et al. (1955) found experimentally that this increase is equal to the flow through the fistula if this is less than 20% of the cardiac output. With fistula flows greater than 27% of the control cardiac output, the increase in cardiac output was not sufficient to compensate for the fistula flow. If plasma expander was infused, the cardiac output increased enough to compensate for the fistula flow. In patients with chronic fistulae the cardiac output is often increased as confirmed with ballistocardiography, Fick principle and dye dilution methods (Binak et al. 1960; Cohen et al. 1948; Warren et al. 1951a). With occlusion of the fistula the cardiac output falls immediately to the same values which can be measured after the operative closure of a fistula (Nickerson et al. 1951).

In cases of very large arteriovenous fistulae, cardiac failure eventually occurs, giving the usual manifestations such as cardiac dilatation, fluid retention, peripheral edema, pulmonary edema, ascites etc. Cardiac decompensation may occur within few hours after the experimental construction of an aorto-vena caval fistula or after many years in cases of traumatic fistulae in patients (Holman 1937; Vollmar 1964; Heberer 1961; Dahlbäck 1970). In some cases cardiac decompensation occurred more than 50 years after acquiring the fistulae.

The blood volume was studied in patients before and after the closure of the arteriovenous fistulae (Warren et al. 1951b) and found to be lowered significantly after operation of larger fistulae.

Local circulatory effects. Signs of affected local circulation leading to ulceration or gangrene have been reported by Dramez et al. (1962) in a case of congenital arteriovenous fistula and by Kornfält (1957) in a traumatic fistula. In these and other similar cases the reason for ulceration may partly be venous insufficiency. Gangrene is known to have occurred in some cases where an arteriovenous fistula was treated by ligation of the central artery (Breschet 1833).

Dilation of the vein leading from an arteriovenous fistula is a well-known phenomenon. The vein wall also increases in thickness (Holman 1937; Petrovsky & Milonov 1967; and others). Histologically there is an increase in thickness of the median coat causing the vein to resemble an artery.

The artery is found to be dilated in many cases of arteriovenous fistula, as reported already by William Hunter (1757) and verified clinically and experimentally (Callander 1920; Holman 1924; Mörl 1954; Vollmar 1964; Ingebrigtsen 1965; Petrovsky & Milonov 1967). The degree of dilation has some relation to the size of the fistula opening and to the blood flow through it. Ingebrigtsen (1965) found experimentally in dogs a hypertrophy of the median coat in the artery proximal to an arteriovenous fistula within the first 15 months after its establishment. A thinning of the wall leading to arterial aneurysms with the risk of rupture is described in long-standing cases (Breschet 1833; Vollmar 1964). Petrovsky & Milonov (1967) found in experimental fistulae an early increase in muscle fibres, extracellular fibrosis and, later, dystrophy of the elastic fibres and diminution of the vasa vasorum network.

The effects of Cimino-Brescia arteriovenous fistulae in dialysis patients has been studied in many dialysis centres and was the topic of a roundtable discussion at the meeting of the European Dialysis and Transplant Association in 1968 (Walsh 1968).

Klinkmann et al. (1967) measured cardiac output, using the Fick principle, in three patients before the creation of an arteriovenous fistula and five months after, and found an increase up to greater than three times the original value. They did not find any signs of heart decompensation. The most comprehensive study of circulatory state in patients with fistulae was published by Lazorthes (1969). He analyzed both local and general effects. In 13 patients cardiac output was measured before and after compression of the fistula using a dye-dilution method. A mean decrease of 11.8% was found. No significant change in mean right auricular pressure or pulse rate could be registered.

Sill et al. (1969) examined 7 patients, four of whom had subcutaneous fistulae. He found a decrease in cardiac output after fistula compression of 1.4–3.4 l/min (mean 3.0 l/min, i.e. 16.4%). No significant effect was recorded upon pulse rate and venous pressure. Johnson & Blythe (1970) studied similar parameters and found in eight patients a mean decrease in cardiac output of 0.65 l/min (6.4% of cardiac output with fistula open). Menno et al. (1967) found a decrease in cardiac output averaging 18.4%.

On the other hand Verberckmoes et al. (1967) and Heidland et al. (1967) did not find any consistent

changes in cardiac output on compression of the fistula, the average change not being significant.

The changes in cardiac output found by various authors have not been related to the original size of the fistula opening.

Treatment of arteriovenous fistulae

Principles for the treatment of arteriovenous fistulae have undergone a change (fig. 4). Initially, the same treatment was used for arterial aneurysms and arteriovenous fistulae. The "old method" of Antyllus meant that the diseased part was incised after the application of a tourniquet, the aneurysmal sac opened, the tourniquet released and probes introduced into the bleeding vessels. These were dissected free and ligated, the ligatures brought out through the wound. Due to

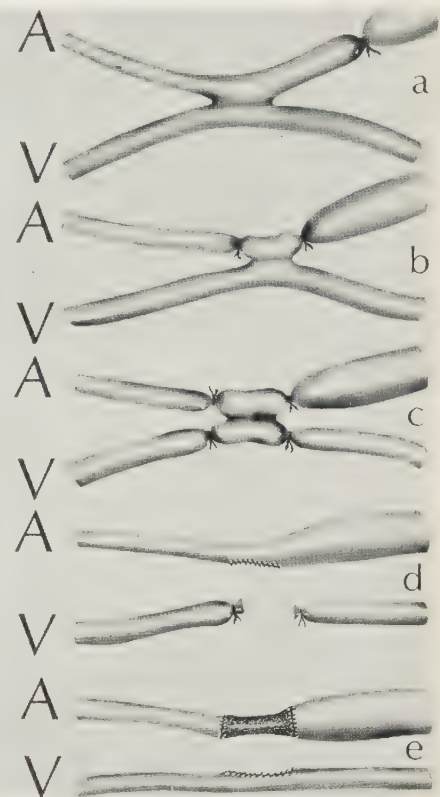


Fig. 4. VARIOUS TECHNIQUES FOR THE TREATMENT OF ARTERIOVENOUS FISTULA

- a Proximal ligation, "Hunterian" ligation.
- b Double ligation of the artery, proximal and distal to the fistula.
- c Quadruple ligation of the arterial and venous limbs.
- d Lateral suture of the artery, ligation of the vein.
- e Reconstruction of both artery and vein.

complications with immediate and late bleedings, this method was replaced by "Hunterian ligation" of the artery central to the aneurysms. In arteriovenous fistulae this method gave bad results. Breschet (1833) referred to a case where central ligation lead to gangrene and to death of the patient. He recommended ligation of the artery both above and below the fistula. In spite of his and similar reports, central ligation was used by several surgeons even during the Boer War. Central ligation of the artery is justified only in cases of multiple congenital fistulae as an alternative to amputation and in cases of intracranial fistulae. Even "double" ligation i.e. ligation of the artery above and below the fistula has the disadvantage that unnoticed collateral arteries might keep the fistula open.

"Quadruple" ligation, i.e. ligation of both artery and vein above and below the fistula, developed as the standard method of treatment during World War I (Reid 1925) and was still the approved technique during World War II (Bigger 1944). It should preferentially be combined with excision of the fistula region. Quadruple ligation of large vessels should not be performed until sufficient time, 3—6 months, has passed for the development of sufficient collateral circulation. It is still a good method for the treat-

ment of fistulae in peripheral vessels such as the radial and ulnar arteries.

With the development of improved vascular surgical technique, new principles for fluid replacement, the availability of anti-coagulants and improved transport facilities during the latter part of World War II (de Bakey 1946) the Korean War (Hughes et Jahnke 1958) and still more in the Vietnam conflict (Fischer 1967, Chandler & Knapp 1967), vascular injuries are treated with primary repair of the vessels. This often prevents the development of arteriovenous fistulae. Manifest fistulae are treated early with reconstruction of the artery by lateral suture, closure of the artery using an excised part of the vein sutured from the inside as in endaneurysmorrhaphy (Matas 1903), or replacement of the diseased artery with synthetic material or an autologous vein graft. The vein should be repaired, if possible, in fistulae of the leg. The same principles of treatment are used in civilian vascular injuries (Drapanas et al. 1970, Vollmar 1967).

In treatment of a long-standing and large arteriovenous fistula, the acute increase in peripheral resistance may lead to heart decompensation. Immediate venesection can be considered in such cases (Rau & Heberer 1961, Dahlbäck 1970).

CLINICAL MATERIAL

Since February 1967 the Cimino-Brescia fistula has been used routinely in this hospital for patients taken to haemodialysis for chronic renal failure. Patients who previously had a Quinton-Scribner shunt had this shunt replaced by a fistula when complications occurred to the shunt. At the present time (April 1972) all 44 patients on chronic haemodialysis have Cimino-Brescia fistulae.

The good experience with the fistula for dialysis prompted its use to facilitate the administration of a cytostatic drug, Estracyt^R (Jönsson 1969) which has a tendency to give thrombophlebitis when injected intravenously.

Consequently the technique was also applied for patients receiving long-term intravenous therapy where the veins were poor or previously destroyed by venipuncture.

Our clinical experience of the construction and use of Cimino-Brescia arteriovenous fistulae will now be reported. In evaluation of the clinical results only patients operated upon by the present author will be included. Some of these patients have been operated several times and one or more of the operations may have been performed by some other surgeon.

CONSTRUCTION OF ARTERIOVENOUS FISTULAE ACCORDING TO CIMINO-BRESCIA

Anatomical notes

The arteries of the upper extremity have a fairly constant distribution (Fig. 5) which can be studied in the standard anatomical text-books. The brachial artery divides at the elbow joint into two main branches, the radial and the ulnar arteries. The radial artery continues in the direction of the brachial artery. Shortly after its origin it is accompanied by the superficial branch of the radial nerve, overlies the pronator teres muscle and is covered by a duplication of its fascia. It is situated in the groove between the brachioradialis and the flexor digitorum muscles partly covered by the brachioradialis. In the distal third of the forearm the radial artery is covered only by the antebrachial fascia and no longer accompanied by the

nerve. Distal to the radial styloid process the artery turns dorsally covered by the flexor pollicis brevis and abductor pollicis longus tendons and appears in the foveola radialis, "Tabatière". The ulnar artery is generally larger than the radial. It turns medially and gives off the common interosseous artery. After this, it is usually smaller than the radial artery. In its passage distally, the ulnar artery is covered by the flexor digitorum communis and flexor carpi ulnaris muscles and is accompanied on the medial side by the ulnar nerve. In the distal fourth of the forearm it is situated more superficially but is still covered by muscles and is more difficult than the radial artery to dissect free and use for anastomosis without kinking the artery.

The arteries of the forearm have a rich net of collaterals, in the hand they form the deep and superficial palmar arches.

The veins of the arm form two systems, the deep and the superficial. The deep system generally consists of two accompanying veins to each artery. These two veins communicate with each other forming a plexus around the artery. The superficial system is larger and more important for return of venous blood. There is a considerable surplus of veins, and the conditions for venous return of blood from the arms are good. Disturbed venous return from the arm is very uncommon. The anatomy of the superficial veins shows great variations (Fig. 6-7). In general the venous plexus of the back of the hand forms the cephalic vein which passes along the radial aspect of the forearm, communicates with the medial cubital vein and continues in the lateral muscle groove of the upper arm penetrating the fascia at the margin of the deltoid muscle and enters the axillary vein. The basilic vein originates from the dorsal plexus on the ulnar side. It passes proximally on the ulnar dorsal side of the forearm, turns ventral to the ulnar humeral epicondyle, communicates with the median cubital vein and passes in the medial muscle groove where it penetrates the fascia in the middle part of the upper arm to flow into the medial brachial vein. The cephalic and basilic veins are normally rather thick-walled. They lie under the subcutaneous fascia, are movable and easily dissected free. Both vary considerably in size and they may be

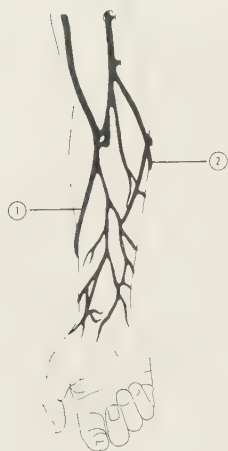


Fig. 5. MAIN ARTERIES OF THE FOREARM AND HAND.

The brachial artery divides into the radial artery (1) and the ulnar artery (2). The ulnar artery gives off the common interosseous artery (3). The radial and the ulnar arteries normally form the volar arches (4).

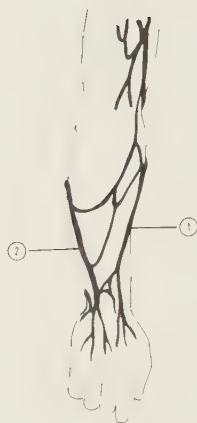


Fig. 6. MAIN VEINS OF THE FOREARM DORSAL ASPECT.

The cephalic vein (1) arises from the radial part of the dorsal venous plexus of the hand. The basilic vein (2) passes on the ulnar dorsal side of the arm.

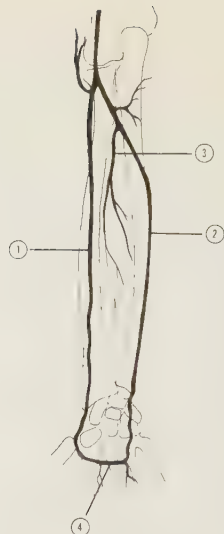


Fig. 7. MAIN VEINS OF THE ARM, VOLAR ASPECT.

The cephalic vein (1) passes on the radial side, communicates with the veins of the cubital fossa, continues on the upper arm to reach the axillary artery at the medial margin of the deltoid muscle. The basilic vein (2) passes ventral to the medial humeral epicondyle, communicates with the cubital veins and penetrates the fascia in the middle of the upper arm to join one of the brachial veins. Great normal variations.

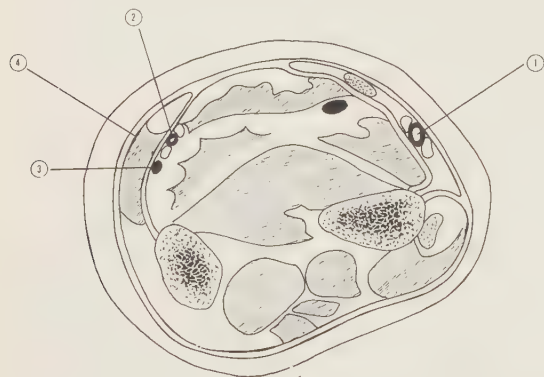


Fig. 8. CROSS-SECTION OF THE LEFT FOREARM IN THE NORMAL REGION FOR A SUBCUTANEOUS ARTERIOVENOUS FISTULA.

The radial artery (1) lies immediately underneath the superficial antebrachial fascia, accompanied by its two veins. The ulnar artery (2) lies deeper, partly covered by the flexor carpi ulnaris muscle (4) and is accompanied by the veins and the ulnar nerve (3).

doubled or missing. The veins of the rich plexus on the ventral side of the forearm are often extremely thin-walled, are many times fixed to the skin and easily kinked. Their course is often very irregular and they are generally unsuitable for constructing an arteriovenous anastomosis.

Some nerves should be considered important in order to prevent injury to them. The median nerve at the elbow level lies medially and close to the brachial artery. It passes in front of the ulnar artery where the common interosseous artery takes off. The ulnar nerve accompanies the ulnar artery in the middle and distal thirds of the forearm. The superficial branch of the radial nerve accompanies the radial artery in the proximal third of the forearm and one or more of its branches penetrate the antebrachial fascia and pass on the lateral aspect of the radius. These branches should be considered in the construction of the fistula between the radial artery and the cephalic vein.

In the leg suitable arteries for anastomosis are found behind the medial malleolus, the posterior tibial artery, and on the dorsal side of the foot, arteria dorsalis pedis. Suitable veins are found in front of the medial malleolus, the great saphenous vein, and in the plexus on the dorsal side of the foot.

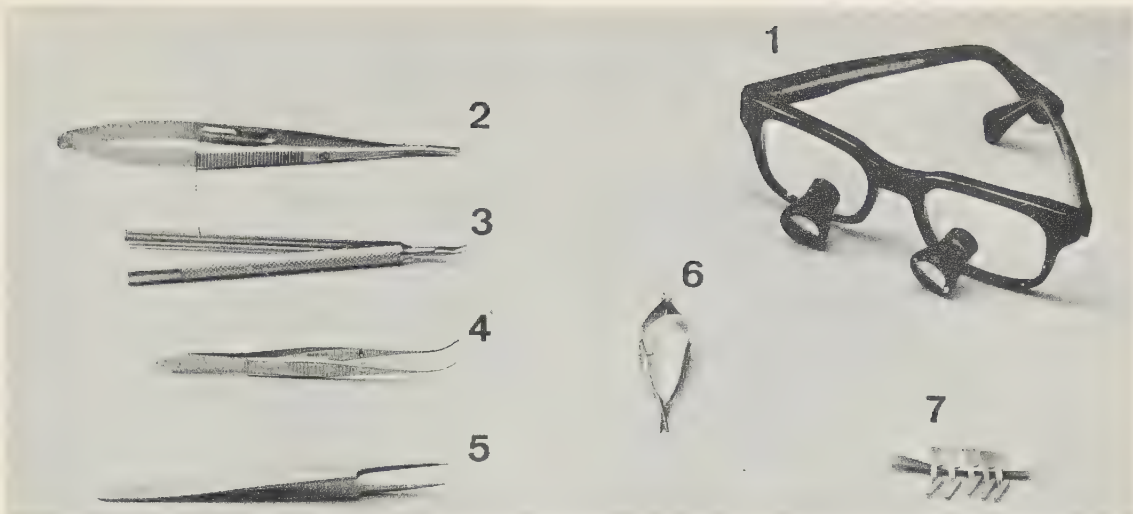


Fig. 9. INSTRUMENTS USED FOR ARTERIOVENOUS FISTULA OPERATION.

The ophtalmic magnifier⁽¹⁾ gives 2x magnification (Carl Zeiss, Germany). In the left row, we see from the top a needle holder for microsurgery (XDJ-445, Snowden-Pencer, USA)⁽²⁾. Micro needle holder, round type (18100 F L Fischer, Germany)⁽³⁾. Curved 12 cm iris forceps⁽⁴⁾ and watchmaker's forceps⁽⁵⁾. In the middle isis scissors⁽⁶⁾, right below small vascular clamps (17022/2 F L Fischer, Germany)⁽⁷⁾.

Equipment

The special instruments used are shown in Fig. 9. Magnifying spectacles giving double magnification (manufactured by Carl Zeiss, Oberkochen, Germany) have been used. Needle holders can be of the Castroviejo or Barraquer types for eye surgery and microvascular surgery. For the very fine needles sometimes used, a special micro needle-holder, round type (manufactured by F L Fischer, Freiburg, Germany) is preferred. Straight and curved ophthalmic forceps, watchmaker's pointed forceps and a fine pointed iris scissors should be available. 6/0 or 7/0 teflon coated polyester fibre (Ethiflex^R, needle C1 or better BV1, manufactured by Ethicon Inc., Somerville, N. J. USA) is preferred as suture material for normal sized vessels. For vessels smaller than 2 mm, external diameter, 9/0 monofilament nylon (Ethilon^R, needle BV2, Ethicon) is used.

Preoperative planning

The most suitable place for the arteriovenous anastomosis is 4–5 cm above the radial styloid process where the radial artery and the cephalic vein normally are easily available. The radial artery can easily be dissected free at any level, even in the Tabatière. The ulnar artery is also easily found in the distal third of the forearm, although it lies deeper and is more protected than the radial. The ulnar artery is less

available more proximally. The brachial artery is also easily dissected free around the elbow level for anastomosis to the cephalic vein or to a free vein graft.

The cephalic vein can normally be dissected free easily at any place along its entire course. It can be used for anastomosis at any level, even in the overarm. The basilic vein is generally situated more dorsally than the cephalic and it is technically more difficult to explore this vein. Sometimes it can be brought to the ulnar artery for side to side anastomosis, other times it must be cut and the anastomosis made end to end or end to side. Arteriovenous fistulae can also be made in the leg between the posterior tibial artery and the internal saphenous vein 5–10 cm above the medial malleolus, usually as end to side anastomosis, or between the arteria dorsalis pedis and the vein on the dorsal side of the foot. However, the function of a fistula in the leg is less satisfactory than in the arm. In the absence of suitable veins in the lower arm, the use of a free graft of saphenous vein between the radial, ulnar or brachial artery and any available superficial vein at any level or a deep vein above the elbow level is preferred.

The arteriovenous fistula is preferably done on the non-dominant arm. If the arteries of the arm have not been previously operated upon and if there are palpable pulses, a suitable artery is easily found.

Sufficiency of the collateral circulation should, however, be tested. Capillary refill should be demonstrable in the thumb when the radial artery is compressed. In most young patients obvious pulsations are palpable in the artery distal to the point of compression (Henle-Coenen's sign). Reactive hyperaemia should be demonstrable in the fingertips when, after a few minutes of total arterial compression using an Esmarch's bandage, the bandage is released but compression of the artery in question is maintained (Moszkowitz's sign). If one or more arteries of the arm have been ligated or previously used for shunts or fistulae preoperative brachial angiography is recommended (see below). The condition of the vein is more critical. In most cases the cephalic vein can be demonstrated using venous compression. In many cases, for example, in obese or overhydrated patients and in patients on oestrogen therapy, the condition of the vein can not be evaluated until after surgical exploration. If the vein has been recently punctured and if there is a subcutaneous haematoma at the site of planned operation, some other site should be used. Phlebography is of limited value for the evaluation of veins for anastomosis (see below).

Anaesthesia

Plexus block anaesthesia, either as an axillary block or as a brachial block, is preferred. Local infiltration anaesthesia can also be used but dissection is then more difficult to perform and vascular spasm is more frequent. Regional intravenous anaesthesia has been used in one case. General anaesthesia was used in children and for by-pass grafts using saphenous vein.

Surgical technique

In the standard case, a 2–4 cm transverse incision is made 4–5 cm above the wrist on the radial side of the non-dominant arm. The vein is first dissected, it is freed for at least 3–4 cm, cutting the subcutaneous fascia as far as possible saving collateral vein branches if possible. If the lumen of the vein is inadequate or if it has been damaged by thrombosis, a new vein must be found. The fascia covering the radial artery is cut longitudinally so that 3–4 cm of the artery is exposed avoiding injury to the plexus of accompanying veins. The adventitia of the vein is dissected only 1–2 mm around the place of anastomosis, somewhat more is dissected from the artery. If the vessels can be brought together without tension the anastomosis is made side-to-side, otherwise one

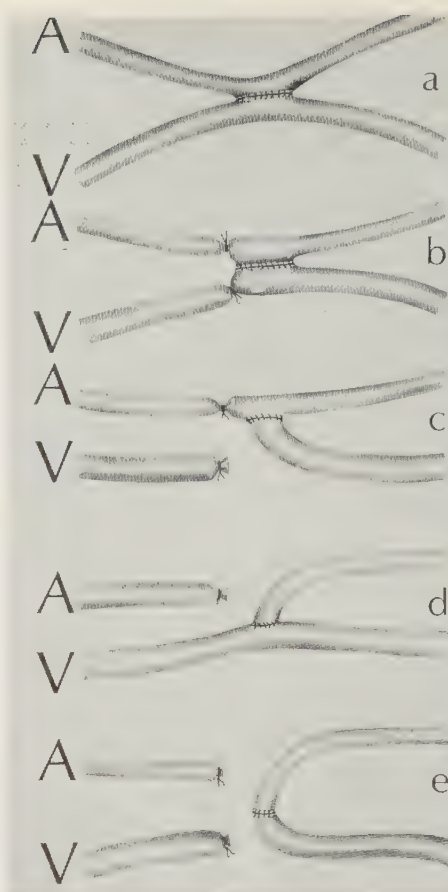


Fig. 10. VARIOUS ANASTOMOSIS TECHNIQUES FOR THE CONSTRUCTION OF CIMINO-BRESCIA ARTERIOVENOUS FISTULAE.

a side-to-side anastomosis.

b side-to-side anastomosis with ligation of both artery and vein distal to the fistula.

c side-to-end anastomosis with ligation of the artery distal to the anastomosis.

d end-to-side anastomosis.

e end-to-end anastomosis.

or both vessels can be cut and the anastomosis made end-to-end, side-to-end or end-to-side. In most cases of side to side anastomosis both artery and vein are left open in both directions. The vessels are closed using 2 mm broad rubber bands or non-crushing vascular clamps. A longitudinal incision is made in each vessel and extended to a length of 3–5 mm. Local thrombendarterectomy is performed if atherosclerotic plaques are present in the artery. The vessels are flushed with a freshly prepared 1:100 dilution of Heparin solution (5000 IU per ml, AB Vitrum,



Sweden) in saline (0.15 M sodium chloride). We make sure that there is a free flow proximally in the vein and free blood flow from both directions in the artery. A stay suture is made in the anterior wall of each vessel (Fig 11). The anastomosis is started by putting a few sutures into the adventitia of the artery and vein 1–2 mm distal to the incision (Fig 12) after which the posterior wall is sutured from the inside using a continuous over and over suture taking the finest possible bites and using 10–15 sutures in 5 mm (Fig 13). When the posterior row is finished we continue proximally with one or two sutures from adventitia to adventitia (Fig 14) and the anterior wall is then sutured using the same thread. The vessels are filled with Heparin solution just before finishing the anastomosis (Fig 15). The occluding bands or clamps of the vein and artery are released and the suture line is slightly compressed for at least 2–3 minutes. If there is a leakage from the anastomosis after that time a thin strip of oxydized cellulose (Spongostan^R, AB Ferrosan, Sweden) is temporarily laid over the suture line. When the occlusion is released the vein is filled and a distinct turbulence can be felt (Fig 16). The vein is somewhat constricted at the site of the temporary proximal





closure, but it usually distends within a few minutes. A final check is made that the vein is not kinked proximally by fascial fibres. The skin is closed without using subcutaneous sutures. The wound is sprayed with Nobecutan^R (AB Bofors, Sweden) or a thin strip of gauze is glued over the wound. The bandage must under no circumstances exert any pressure. A light dorsal plaster splint can be used if the patient is confused and restless. The arm may be placed about 10 cm above the level of the heart for 12 hours to minimize the oozing of blood. After the operation a murmur can often be heard over the anastomosis. If a murmur has not appeared within 12 hours after operation the anastomosis is most probably occluded and reoperation is to be made.

In performing an end-to-end anastomosis, vascular clamps are applied proximally, the vessels ligated far distally with 5/0 silk and cut obliquely about 60°. The anastomosis is made over an inlying splint of plastic tubing and interrupted sutures are used. The splint is withdrawn immediately before the last two knots are tied. Even in end-to-end anastomosis a thrill is palpable and a murmur is heard, although not as impressive as in side-to-side anastomosis.



If the patient does not need his fistula any longer, the artery can usually be saved in cases where the anastomosis was made to the side of the artery. The vein is cut and ligated and the opening in the artery is closed using a simple continuous suture over and over.

If the fistula has grown too large, the distal branches of the artery and the vein should be ligated and the fistula opening narrowed using a few sutures through and through. It is also possible to put a strip of dacron web around the vein to produce a narrowing.

Puncture-technique

For haemodialysis a wheal of 0.5% mepivacain chloride (Carbocain^R, AB Bofors, Sweden) is raised in the skin, a one mm long transverse skin incision is made with a pointed knife and the vein cannulated using a thin walled metal needle, Gauge 14. (2.1 mm O.D.) The proximal cannula is introduced first, the calculated amount of Heparin is injected and this cannula is used as "vein" bringing blood from the machine back to the patient. The distal cannula, used as "artery", is preferably introduced pointing distally. After dialysis treatment is finished the distal cannula is withdrawn first and compression is applied for some minutes at the site of puncture and just *distal* to it to prevent leakage and haematoma formation. A bandage using slight compression is applied for 6–12 hours.

For taking blood samples and giving injections a fine hypodermic needle is used. For intravenous infusions metal or teflon cannulae are used. It has been a routine not to make the injection closer than 5 cm from the fistula as there is a risk of intraarterial injection. The injection should not be started until venous compression is released. When the injection is finished, the needle should be left in place 5–10 seconds so that the flow of blood has flushed away the injected drug. After the needle has been removed slight compression is applied for a few minutes. If a new cannulation has to be made within 1–2 hours venous compression should not be used, otherwise there may be haematoma formation at the site of the previous puncture.

Patients

The material consists of 181 patients with Cimino-Brescia fistulae divided into three groups. The first, 103 cases, consists of patients with uraemia treated with haemodialysis. In the second group, 51 cases,

the fistula was made for cytostatic treatment of prostatic carcinoma. In the third group, 27 cases, the fistula was created in an attempt to facilitate intravenous therapy most often after major surgical operations.

RESULTS

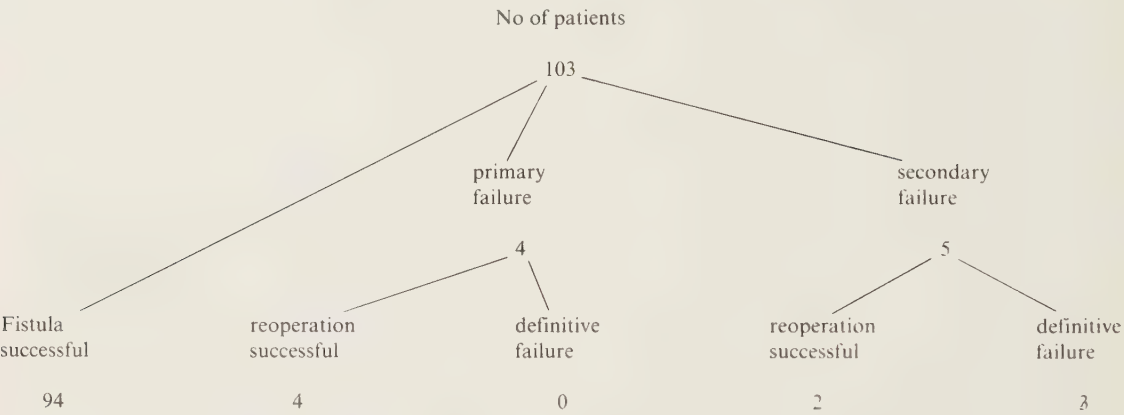
The standard anastomosis technique was side-to-side between the radial artery and cephalic vein preferably in the non-dominant arm and the opening was made 3–5 mm long. In four consecutive early cases end-to-side anastomosis, and in two side-to-end anastomosis, were performed from the radial artery to the cephalic vein. After that, deviations from the standard technique were made only when this was impracticable. In 12 cases side-to-side or side-to-end anastomoses were made from the ulnar artery to the basilic vein. In five cases where side-to-side anastomosis was impossible the anastomosis between radial artery and cephalic vein was made end-to-end. Small volar veins were used in 12 cases where no large vein was available. In five patients bridge grafts were made using a saphenous vein segment interposed between the radial artery and the basilic vein. The graft was laid in a loop subcutaneously in the forearm. No fistulae were made in the upper arm or in the leg.

The functional results in 103 patients with uraemia is shown in Table I. In all patients it was possible to perform a functioning fistula, although some had to undergo several operations.

Operations where continous function of the fistula was achieved are called successful. Patients in whom no fistula could be created or where the fistula stopped functioning within the first postoperative 24 hours are regarded as having primary failure. Fistulae with primary function that ceased to function later than 24 hours postoperatively are called secondary failures. Patients in whom long-term function of fistula could not be reached are called definitive failures.

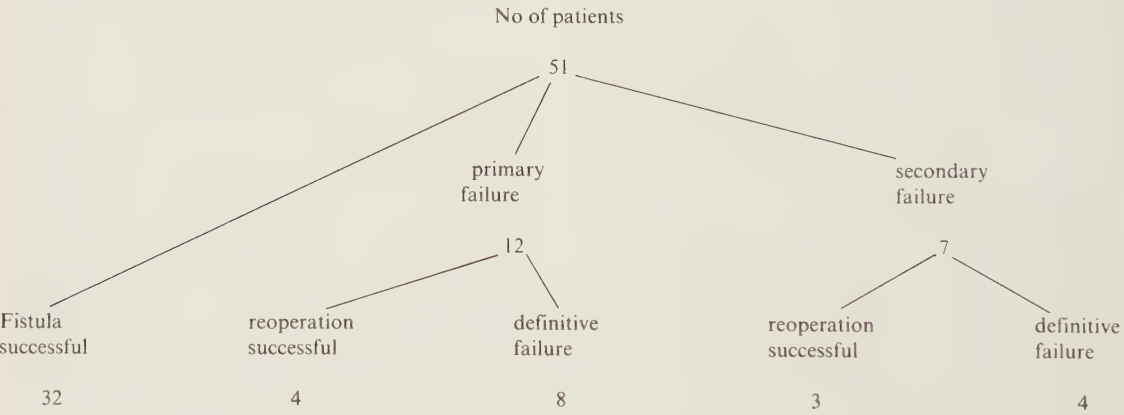
Three patients had definitive failure. One of them was a 42 year-old woman with polycystic kidney disease. Six weeks after operation she developed a thrombosis in the fistula and was reoperated upon. The new fistula clotted after three weeks and so did a third fistula. A Quinton-Scribner shunt was made but this coagulated after every dialysis. The patient was given dicumarin which did not prevent shunt clotting. She died shortly afterwards of a cerebral

TABLE I. Patients with Cimino-Brescia fistulae having uraemia.



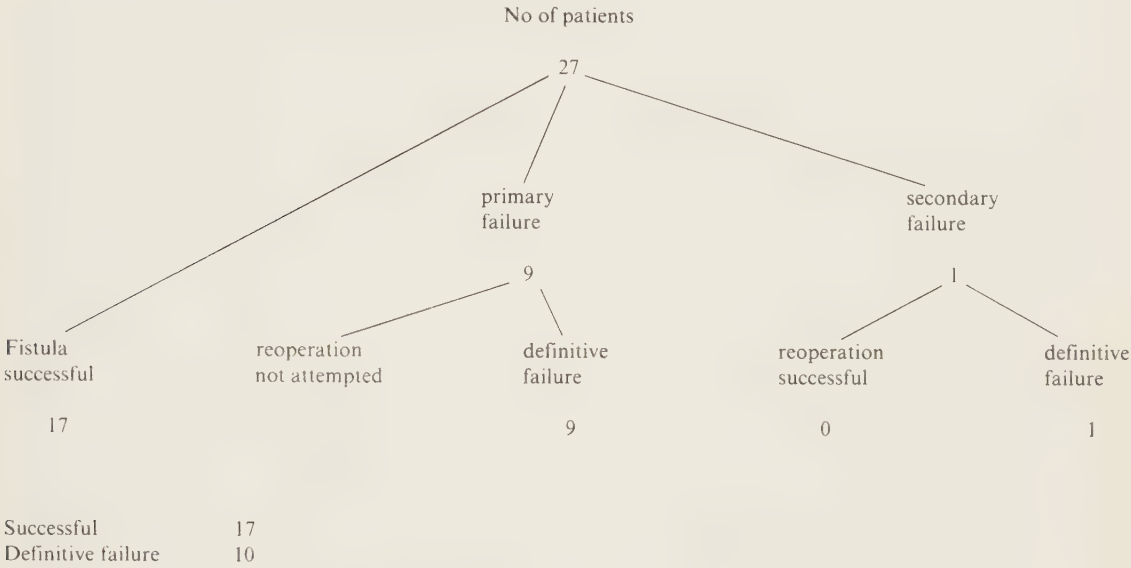
Successful $94 + 4 + 2 = 100$
Definitive failure 3

TABLE II. Patients with Cimino-Brescia fistulae made for cytostatic treatment of prostatic carcinoma.



Successful $32 + 4 + 3 = 39$
Definitive failure 12

TABLE III. Patients with Cimino-Brescia fistulae created for intravenous therapy (prostatic carcinoma excluded)



bleeding probably arising in a cerebral cyst. One of the patients with secondary failures had to be operated upon with construction of fistulae four times in four years. These operations were primarily successful every time but complications with haematoma formation led to later closure. She was given a bridge graft from the radial artery to a vein at the elbow (see angiogram Fig. 30). She was cachectic with muscular atrophy and her vessels were very narrow and fragile. Even the latest fistula has clotted but she has received one unsuccessful and one successful kidney transplant.

The third patient died due to complications to his uraemia not related to the fistula. He had repeated fistula clotting and no functioning fistula at the time of his death.

In one patient with hypoplastic veins the fistula was functioning unsatisfactorily, (see angiogram Fig. 24), a temporary Quinton-Scribner shunt was made in the other arm and in the course of time the fistula has increased so that it can now be used for dialysis after the external shunt has clotted.

In 7 patients the fistula was working but cannulation of the veins was difficult and a second fistula was made in the other arm, giving more sites for cannulation.

Nine patients had previously had Quinton-Scribner shunts which coagulated and were successfully replaced by fistulae.

The oldest patient in the uraemia group was 78, youngest 7. Our experience with the fistula for dialysis in three girls of 14, 13 and 7 years of age have previously been reported (Lindstedt, Lindergård & Lindholm 1971).

The second group is presented in Table II. The results are considerably less satisfactory than in the first group. It was possible to create a fistula in only 43 of the 51 patients. In 7 of the 12 definitive failures the veins were abnormal and it was necessary to use a vein with thrombophlebitic changes or a small thin-walled vein at the volar side of the wrist. Three of the secondary closures occurred in patients with abnormal veins. However, one primary failure and four secondary closures occurred in patients who had macroscopically normal veins at the time of operation. Long-term function was only achieved in two of the cases in whom an undamaged cephalic or basilic vein was not available for anastomosis.

The third group consists of patients where the fistulae were made to facilitate or make possible intravenous

treatment. In 17 cases major surgical operations were performed or planned, in 10 long-term treatment for other conditions was given. The results will be found in Table III. The operation was successful in 17, in seven out of nine patients with primary failure no normal large vein was available. The operation was successful in four cases where small volar veins were used. The youngest patient was a boy of 9 months in whom the fistula was made in an attempt to facilitate the repeated blood transfusions necessary for the treatment of thalassemia major. The fistula occluded after six days, an attempt to make a fistula on the other arm failed.

A bridge graft was attempted twice in patients with prostatic carcinoma. One failed early, the other after 3 weeks. Bridge grafts in 3 uraemic patients were all primarily successful, in two secondary failure occurred.

Six of these patients had their fistula repaired when it was no longer required. In two of them quadruple ligation was made and in four lateral suture of the artery or transvenous endaneurysmorrhaphy according to Matas (1903).

Clinical use of the fistula

The use of the fistula for hemodialysis entailed some technical problems during the first months of our experience in this hospital. Several doctors and nurses were very reluctant to accept the idea of the new type of shunt. The initial difficulties were, however, overcome, and with increased experience among the nursing staff in the dialysis unit the rate of unsuccessful punctures has become small. Problems are mainly limited to the first weeks after start of dialysis treatment and to patients with very small veins. A blood pump is necessary for the dialysis and flows of up to 300 ml per minute can be obtained from most patients. Using a parallel flow disposable dialyzer (manufactured by AB GAMBRO^R, Lund, Sweden) the blood flow received from the fistula is rarely the limiting factor for how fast the dialysis can be driven. The rate of dialysis of small molecules and the risk of dysequilibrium with cerebral oedema most often determines which blood flow should be used.

In most cases the fistula veins have not been punctured during the first week after operation and in many cases they have been saved much longer. In one exceptional case the fistula was used for dialysis two days after it was constructed.

For intravenous injections the fistula veins have been used 1–2 weeks after operation in most cases. The veins have been saved longer in some cases where the vessels were abnormal at the time of operation. Fine needles have been used in most cases and short-cut needles are preferable. No special problems are connected with the use of the arterialized veins. Injections are given slowly and venous spasm, which is observed in patients given cytostatic drugs into non-fistula veins, is seen very infrequently.

Blood sampling using the arterialized veins is easily performed. In the postoperative period after kidney transplantation, for example, puncture of the fistula veins is preferred to puncture of other veins. Intravenous therapy has been given using the same indwelling cannula for up to one week. Measurement of PO_2 and PCO_2 has been made in blood from the fistula veins as arterial blood.

Complications

Complications related to the fistula operation as such have not occurred. In some cases a small haematoma has developed in the operative wound but abscesses or wound sepsis have not been observed. A degree of swelling of the dorsal side of the hand has been present in the early postoperative period in some cases. Persistent swelling of the veins of the dorsal side of the hand has been annoying to some patients and ligation of the vein distal to the fistula has been performed in two cases.

In four patients having postthrombophlebitic changes of the veins used for anastomosis with stiff vessel walls and insufficient run-off through the veins, a violent reaction with reddening and swelling of the skin overlying the vein appeared as in severe thrombophlebitis. The fistulae worked, however, and the local symptoms subsided during the following two weeks.

One major complication occurred in a patient who had an arteriovenous fistula constructed from the ulnar artery side-to-side to a small vein at the wrist. The fistula functioned unsatisfactorily and intravenous injections of cytostatic drugs were given with difficulties. One injection was made close to the fistula, probably into the artery which made a loop here. Partial occlusion of distal arterial branches occurred and gangrene of part of the thumb and index finger was the consequence. After this occurrence puncture of the vein closer than 5–6 cm from the fistula has been avoided.

Small or moderate haematomata have arisen after puncture mostly following dialysis. Secondary bleeding from the puncture site has been observed occasionally, but in no case blood transfusion was required. The frequency and amount of post-dialysis bleeding from the puncture site has decreased with increased experience among the staff.

In one dialysis patient an infected haematoma after venipuncture communicating with the fistula vein probably contributed to the patient's death.

Another patient with a similar haematoma was operated upon with resection and ligation of the vein.

Discussion

The original description of the Cimino-Brescia fistula (Brescia et al. 1966) suggested the use of a side-to-side anastomosis. Some authors were less successful with this technique and recommended the use of an end-to-end anastomosis (Sperling et al. 1967; Robson et al. 1969; Lymberopoulos et al. 1970) or a side-to-end anastomosis (Röhl et al. 1968). We started to use the side-to-side anastomosis and found this useful as a standard procedure in cases where it was technically practicable. We created a few side-to-end or end-to-side anastomoses but found no advantages in using these. The end-to-end anastomosis was used where no other technique was possible. Using this technique, vessels lying at a considerable distance from each other can be anastomosed. When either the radial or the ulnar artery was previously used for a shunt or a fistula in the forearm, the other artery was used without hesitation. The new anastomosis was, in these cases, if possible, made to the side of the artery. If the cephalic vein in the non-dominant arm is not available, the cephalic vein in the other arm is tried. If even this is destroyed the basilic vein is looked for. As the basilic vein is less accessible for puncture it has often been left in good condition. It is well suited for anastomosis, generally end-to-side to the ulnar artery. Puncture of this vein for haemodialysis may be difficult but it is most often possible to perform it.

The number of anastomoses deviating from the standard technique is small. In almost all these cases there has been some special reason for the deviation and no conclusion can be drawn concerning the rate of surgical success with the different techniques.

For anaesthesia in the standard operation, plexus block is preferred, generally via the axillary route.

This gives good anaesthesia for a sufficient period of time. Anaesthesia of the whole arm and muscle paralysis makes the operative procedure less uncomfortable for the patient and makes it easier for him to lie still. The tendency for vascular spasm is little probably due to the accompanying sympathetic block. Local infiltration anaesthesia can be used but is less convenient. Regional intravenous anaesthesia was tried once. It gives excellent anaesthesia and the operation is easily performed in the blood-free field. In this case, however, severe venous spasm was present for several hours after operation. It is important to check the free blood flow from the opened vessels and the function of the created anastomosis, and this can not be done if regional intravenous anaesthesia is used. General anaesthesia is preferred for children and it is the best type of anaesthesia if a bridge graft of saphenous vein is performed. In these cases, the plexus block anaesthesia has often passed off when the subcutaneous tunnelling for the graft is to be made.

There is a considerable rate of primary and secondary failures in the second and third groups of patients while the rate of failure in the first group is small. Primary failure may be due to technical factors such as improper handling of the vessels and poor anastomosis technique. It can also be due to changes within the vessels used for anastomosis: arteriosclerosis, insufficient size of the vessels or postthrombotic changes. Morphological changes in the surrounding tissues such as subcutaneous fibrosis or oedema due to overhydration or to oestrogen treatment may be contributing factors. In two cases, pressure from a bandage was the probable cause of early occlusion.

Some of the primary failures can no doubt be explained as being due to technical factors. Some of the primary failures among prostatic carcinoma patients occurred during the early period when a fistula was created too late, the subcutaneous veins having been destroyed by previous injections. Anastomosis was attempted using small volar veins or veins with postthrombotic changes. These were rarely successful.

In the third group of patients, lack of subcutaneous veins was the main indication for the attempts to create fistulae. This is probably the main reason for the rather poor results in this group. In four patients, however, the operation was successful where only very poor veins were available. Intravenous therapy, previously impracticable, was thus made possible.

Arteriosclerotic changes in the artery was rarely an important reason for surgical failure, even in older patients.

Technical and anatomical factors can not, however, offer enough of an explanation for the great difference in the rate of primary and secondary failure between uraemic and non-uraemic patients. It is probable that factors within the primary haemostasis and the coagulation and fibrinolysis systems are more important. It is known that many uraemic patients have a decreased number of thrombocytes and decreased thrombocyte adhesiveness (for ref. see Larsson 1971). This would cause a lesser tendency for fistula clotting and the decreased haematocrit and viscosity of the blood (Walsh 1968) would act in the same direction. On the other hand, increases in factor VIII, fibrinogen and prothrombin-proconvertin are common in these patients and the activators of fibrinolysis in the blood

are often decreased. These changes could be contributory to the repeated clotting of fistulae in some patients in the first group. The patient who also clotted her Scribner shunt repeatedly was shown to have decreased activation of fibrinolysis in the wall of her veins (Prof. Inga Marie Nilsson, Coagulation laboratory, Malmö). Oestrogen treatment also causes reduction of activators of fibrinolysis which could be an important reason for the increased tendency of secondary failure in patients of the second group.

The rate of thrombophlebitis caused by the injections of cytostatic drugs could be decreased considerably after an arteriovenous fistula had been constructed. It was found to be important, even in these cases, to introduce the medication slowly and to wait for some seconds after the injection is finished to pull out the cannula. Otherwise the concentration of drug in the vein may be so great that injury to the intima occurs.

ANGIOGRAPHIC STUDIES IN PATIENTS WITH CIMINO-BRESCIA FISTULAE

By Jüri Kaude & Eric Lindstedt

Angiography has been used extensively in studies of normal and abnormal conditions in connection with Quinton-Scribner shunts. In Cimino-Brescia fistulae, however, only a few reports concerning angiography have been published. Hurwich (1968) reported angiographic findings in three patients with Cimino-Brescia fistulae and demonstrated the cause of dysfunction of the fistula in two cases. Single angiographic examinations have been reported by Lazorthes (1969), Eisinger et al. (1969), Lindstedt (1970) and others.

The present angiographic study had several aims. We wanted to find out if morphological changes in the vessels connected to the Cimino-Brescia fistula could be demonstrated and wanted to study the circulation in these vessels. Some patients had poor fistula function and we wanted to find the cause for this to consider if the condition could possibly be improved by surgical intervention. In patients with complications to previous shunts or fistulae we wanted to study the conditions within the arterial and venous systems to find suitable vessels for a Cimino-Brescia operation. Using phlebography we also wanted to study the flow of contrast medium between the superficial and deep venous systems in the forearm.

Technique

Retrograde percutaneous catheterization of the brachial artery was performed just above elbow level. The skin was prepared and local anaesthesia introduced using 1% solution of mepivacaine chloride (Carbocain^R, AB Bofors, Sweden) containing 10 IU hyaluronidase (Hyalase^R, AB Leo Helsingborg, Sweden) per 10 ml of anaesthetic solution. A polyethylene catheter (PE 160, ID 1.14 mm, OD 1.57 mm) of a length of about 20 cm was inserted. 10–20 ml of Isopaque Cerebral^R (Nyegaard, Oslo, Norway) were injected manually as rapidly as possible. Usually, 10 films in five seconds were taken using an Elema-Schönander cut film changer. In some cases, blood flow through the fistula was studied with 35 mm cine-



Fig. 17. Well functioning fistula side-to-side between the radial artery and cephalic vein. No filling of the artery distal to the fistula. Dilatation of the radial artery and the cephalic vein, the latter is filled both distally and proximally. —————> Incompetent valve immediately distal to the anastomosis. Arterial supply to the hand via the dilated ulnar and interosseous arteries.



Fig. 18. Side-to-side anastomosis between the ulnar artery and the basilic vein, the artery is ligated immediately distal to the fistula.



Fig. 19. End-to-end anastomosis between the radial artery and the cephalic vein. Venous stenosis (* →) about 2 cm from the anastomosis (————→).

fluorography at 75 frames/sec, or with 70 mm fluorography at 6 frames/sec. In most cases, one radiographic series was made with compression of the veins of the upper arm using a blood pressure cuff inflated to a pressure of 30 mm Hg, and manual compression of the axillary artery. With this compression, the blood flow was slowed down and a better demonstration of morphological changes in vessels involved was obtained.

Phlebography was performed by puncture of a subcutaneous vein on the dorsum of the forearm just above the wrist with a teflon cannula, in operated cases just above the fistula. 10 ml Isopaque Cerebral^R

were injected, and films were taken with 0.5 sec intervals for 10 sec.

All phlebographic examinations were performed in volar-dorsal and lateral projections, with and without compression of the overarm. The pressure applied was 50 mm Hg using a blood pressure cuff.

All measurements of vessel diameter etc. were made without compression on films obtained with a geometric magnification of about 1.1 times.

Patients

Twenty-one patients studied with brachial arteriography had a Cimino-Brescia fistula. In three patients, angiography was performed prior to a Cimino-Brescia



Fig. 20. End-to-end anastomosis between the ulnar artery and the basilic vein

operation. Two patients were examined twice, two three times and one patient four times. Thus, a total of 33 arteriographic studies were performed. The time interval between fistula operation and angiography was from 16 days to 3 years.

Phlebography was performed in two patients with fistula and five healthy controls.

Angiographic findings

The most common type of angiographic findings in a patient with a functioning Cimino-Brescia fistula is shown in Fig. 17. The anastomosis was performed side-to-side between the radial artery and the cephalic vein. Some other surgical techniques used are illustrated in the following figures. A side-to-end anastomosis between the ulnar artery and the basilic vein is shown in Fig. 18. The anastomosis in this case was made to work like an end-to-end anastomosis by ligating the artery distal to the fistula. In the case shown in



Fig. 21. Bridge graft of the saphenous vein interposed between the radial artery and the vein at the elbow level. Slight stenosis at the anastomosis (—————>), some post-stenotic dilation of the vein.

Fig. 19 an end-to-end anastomosis between the radial artery and the cephalic vein has been performed. An end-to-end anastomosis between the ulnar artery and the basilic vein is shown in Fig. 20. In a case without suitable subcutaneous veins on the forearm a bridge graft of the saphenous vein was interposed between the radial artery and a vein at the elbow level (Fig. 21).

The diameter of the radial or ulnar artery feeding the fistula varied between 3.5 and 9 mm (mean 5.5 mm: measured 2 cm proximal to the fistula). In several cases other arteries of the forearm were slightly dilated, but an exact evaluation of the other major arteries could not be made as the opposite forearm was not studied and the normal variation of the vessel size on the forearm is considerable. A comparison of the artery diameter in patients with Cimino-Brescia fistula with the diameter of normal arteries in healthy individuals was not made.



Fig. 22. Patient with side-to-side anastomosis between the radial artery and the cephalic vein, which is dilated. Note dilated radial artery (————→) even distal to the anastomosis filled by collaterals developed mainly from the interosseous artery (* —————→) and rich arterial flow to the hand.

By comparing the artery connected to the fistula to the other main arteries of the forearm we had the impression that a more or less marked widening of the feeding artery of the fistula was present in all 16 cases with well functioning fistula. The dilatation of the artery extended from the division of the brachial artery to the anastomosis. In one case it was developed as soon as 16 days after the operation. Arteries on the upper arm were not studied.

The flow rate of contrast medium through the artery used for the anastomosis was increased as compared with arteries supplying the hand. In 11 cases the contrast passage time from the elbow to the fistula

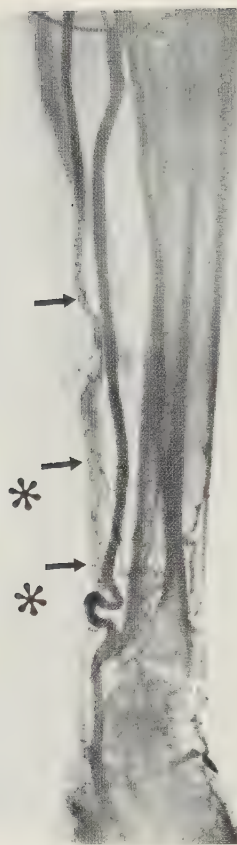


Fig. 23. Lateral view. Thrombotic changes (————→) and slight arterial stenosis proximal to the side-to-side anastomosis between the radial artery and the cephalic vein. Retrograde flow in the incompetent vein distal to the anastomosis (* —————→). Note rich arterial supply to the hand via dilated ulnar and interosseous artery and tortuous collaterals.

could be evaluated and was between 0.5 and 1.0 sec. (mean 0.6 sec.).

The diameter of the vein 2.5 cm from the fistula could be measured in 10 cases. It varied between 2.3 and 10 mm (mean 5.9 mm). In 9 cases the cephalic vein in the forearm emptied in 1.0–4.0 sec (mean 1.9 sec).

Repeated cannulations of the arterialized veins resulted in only small changes detectable by angiography. Aneurysmatic dilation of the vein with an extensive net of arterial venous collaterals around the fistula was present in one patient (Fig 31).

The widths of the fistula openings varied between

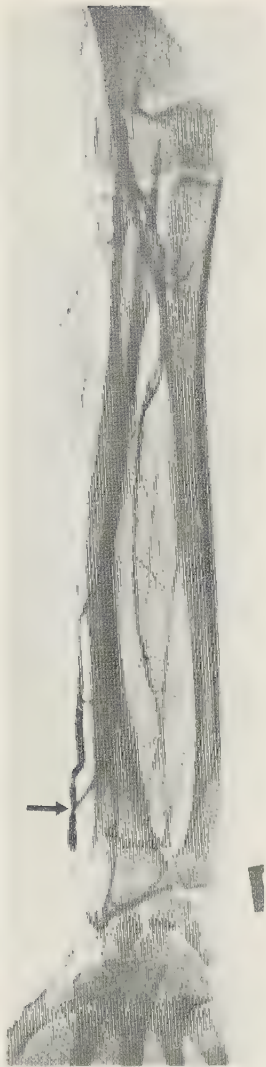


Fig. 24. Side-to-side anastomosis between the radial artery and hypoplastic cephalic vein. Examined by angiography 10 weeks following operation. No localized vascular stenosis.

1 and 4 mm in cases where the diameter could be measured.

Arterial supply of the hand was demonstrated in 7 cases to come from the ulnar and interosseous arteries and in some cases from branches of the radial artery itself. In the remaining cases the fistula consumed so much of the contrast medium that the arteries supplying the hand were not filled. In 3 cases with side-to-side anastomosis the artery distal to the fistula was filled mainly from collaterals (Fig 22) and in the other

cases with side-to-side anastomosis the distal artery was not filled.

In 4 patients, a stenosis was present in the radial artery close to the fistula. The lumen of the artery could be as narrow as 1 mm and the stenotic changes were located within the last two cm above the fistula. Thrombotic changes in the distal stenotic part of the artery were found in one case (Fig. 23).

Three patients were examined because of impaired flow through the fistula. In the first case studied 10 weeks after surgery the blood flow through the artery was reduced and the vein was hypoplastic (Fig 24). The fistula, however, increased slowly and now three years after the operation, it is still used for dialysis.

The second patient with impaired flow was referred to us from an other hospital because the veins from the fistula could not be cannulated for dialysis. Angiography in this patient showed that the anastomosis had been made side-to-side between the radial artery and the cephalic vein and the vein proximal to the fistula was occluded. The distal vein was stenotic and partially obstructed by clots (Fig 25). In this patient, a new fistula was created side-to-side between the ulnar artery and the basilic vein (Fig 26).

In the third patient, with a bridge graft of saphenous vein, thrombosis at the upper vein to vein anastomosis caused an irregular narrowing of the lumen (Fig 27). Heparin treatment did not prevent clotting and occlusion of the fistula.

In some cases even small veins may dilate and adapt themselves to the increased flow and give clinically sufficient fistula function. A young woman with major abdominal, thoracic and skeletal injuries had her subcutaneous veins destroyed by repeated infusions and injections. Therefore the necessary intravenous therapy could not be continued. We succeeded in creating a fistula from the radial artery to a very small volar vein. Following the operation the vein became dilated and could be used for intravenous infusions (Fig 28). The patient recovered after several operations, passed a normal pregnancy and following this the fistula was closed and the artery repaired.

In three cases the flow through the fistula appeared unusually large. In Figure 29 the findings in one of these patients are shown. The artery is dilated to 9 mm and the vein to 11 mm. The patient was reoperated upon, and both the artery and the vein were ligated distal to the fistula and the anastomosis was narrowed with a few sutures. The flow diminished only tempo-

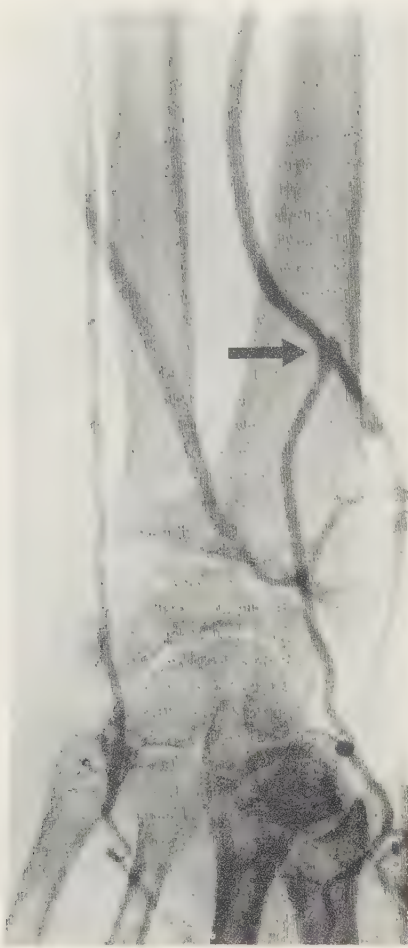


Fig. 25. Angiography 4 weeks after operation. The cephalic vein proximal to the side-to-side anastomosis (—————→) is occluded. Stenosis of the vein distal to the anastomosis.



Fig. 26. The same patients as in figure 25. New anastomosis is made side-to-side between the ulnar artery and the basilic vein (—————→). Angiography 16 days after, the vessels are dilated as sign of well-functioning fistula as compared to figure 25. Retrograde flow in the ulnar artery distal to the anastomosis was present.

rarily and in a new operation a stenosis of the vein was produced using a piece of dacron vascular prosthesis wrapped around the vein 1 cm from the anastomosis.

The second patient with high flow through the fistula had primarily small veins. Two years after operation, however, a very large vein distal to the side-to-side anastomosis had developed. The proximal vein in this case was less dilated (Fig 30 a). The enlarged distal vein was ligated. One year later reoperation with narrowing of the fistula was considered. At preoperative angiography, however, it was found that the cephalic vein was now obstructed. Clotting had probably occurred during the night before examination (Fig

30 b). After several reoperations creating various types of fistulae the patient had a bridge graft of saphenous vein from the radial artery to a vein at the elbow (Fig 30 c). She has later had two kidney transplants, the second functioning well.

In a third patient with fairly large fistula flow (Fig 31) no operative procedure to reduce the flow was performed. This patient died after his second kidney transplantation.

In most cases the vein used for anastomosis was filled with contrast medium both proximally and distally from the fistula. Absence of filling of the distal veins indicates competence of the valves or occlusion of the vein. In some cases the flow of contrast medium



Fig. 27. Thrombotic changes with irregular narrowing of the lumen at the proximal anastomosis between bridge graft of saphenous vein and basilic vein (————→). Anastomosis between the radial artery and the graft is well-functioning (* —————→).

was mainly distal (Fig 32). This retrograde venous flow was well accepted by most patients.

In one patient the radial artery and the cephalic vein of both arms had been used for Quinton-Scribner shunts and were obstructed. At preoperative angiography the radial artery was found occluded and the ulnar artery was important for nutrition of the hand (Fig 33). For this reason, the ulnar artery could not be ligated and the distance between the ulnar artery and the basilic vein was too large to allow side-to-side anastomosis. Therefore the fistula was made between the ulnar artery and the basilic vein side-to-end. Occluded radial arteries were demonstrated in two more patients with previous Quinton-Scribner shunts.

At phlebography in normal controls a good filling of the subcutaneous veins of the lower arm was always found and of the perforating veins to the deep system



Fig. 28. A side-to-side fistula between the radial artery and small volar vein. Twenty weeks following operation the vein is grossly dilated and tortuous.

in the elbow region. On the forearm, however, no filling of the perforating or deep veins was demonstrated (Fig 34). Also in patients with arteriovenous fistula no contrast medium passed over to the deep veins on the forearm.

No complications were observed after angiography.

Discussion

Brachial arteriography using percutaneous catheterization technique (Seldinger 1953) is a simple method to study the vessels of the forearm. If necessary it can be repeated. In patients with Cimino-Brescia fistulae plexus anaesthesia for examination is not required since most of the contrast medium is diverted through the fistula and the small amounts of contrast medium that reach the capillary system do not cause painful reaction. Preoperative brachial angiography is valuable in patients with external shunts or internal

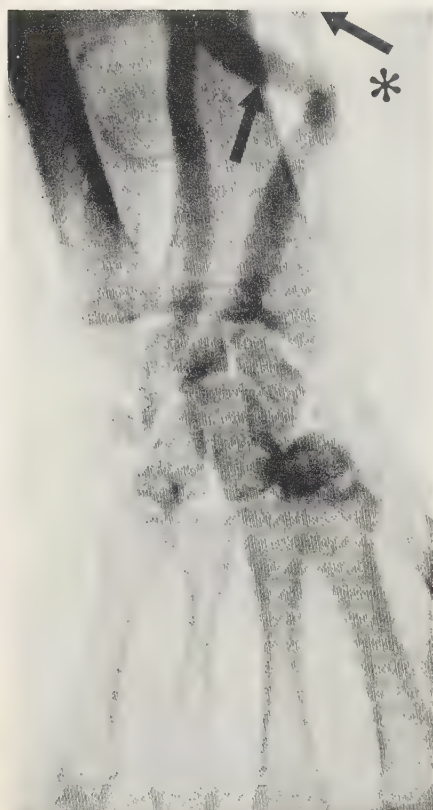


Fig. 29a. Excessive flow through the fistula, dilated radial artery (—————→) and cephalic vein (* —————→) (70 mm frame from serial fluorography made for flow studies).

Fig. 29b. The same patient is restudied after ligation of the distal part of the artery and vein and narrowing of the fistula. The radial artery is still dilated.

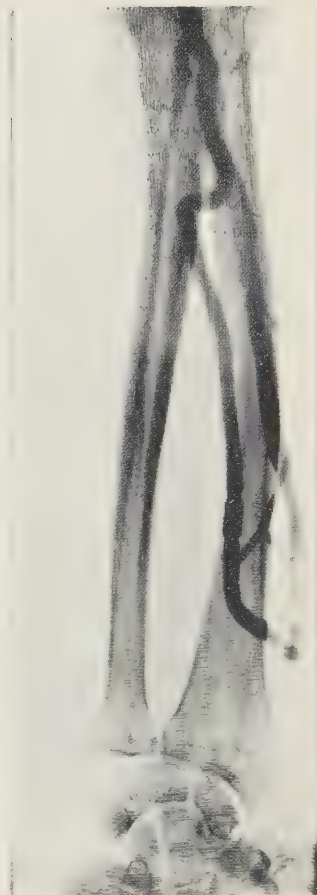


Fig. 29c. After a third operation flow is reduced and the dilation of the artery has diminished.

fistulae that have ceased to function. In such cases it is possible to find out if a suitable artery is available for a new anastomosis. In patients with poor fistula function brachial angiography provides the information required to decide which therapeutic steps should be taken. The size of the arteries, the presence of arteriosclerotic changes and eventual thrombotic occlusions and presence of collaterals are demonstrated. No information, however, can be obtained with regard to the presence and condition of the veins suitable for an anastomosis.

Phlebography could make possible the demonstration of changes such as obstructions and thrombophlebitic changes that would exclude the use of the vein for anastomosis. The method, however, can not be used to distinguish between thickwalled moveable

veins and thinwalled veins fixed to the skin and unsuitable for the fistula.

Dilation of the arteries feeding the fistula occurs in congenital and traumatic arteriovenous fistulae (see page 9 in this volume).

In our examination widening of the artery was indicated in all patients with well functioning fistula. Our studies do not allow any conclusions to be made about the time required for this dilation to develop or for the tendency to further increase of the size of the artery over greater period of time than three years. The dilation of arteries, however, can develop rather early in the postoperative period as shown in one case examined 16 days after the operation.

An aneurysmatic dilation of the artery described by several authors (Vollmar 1964 and others) was not

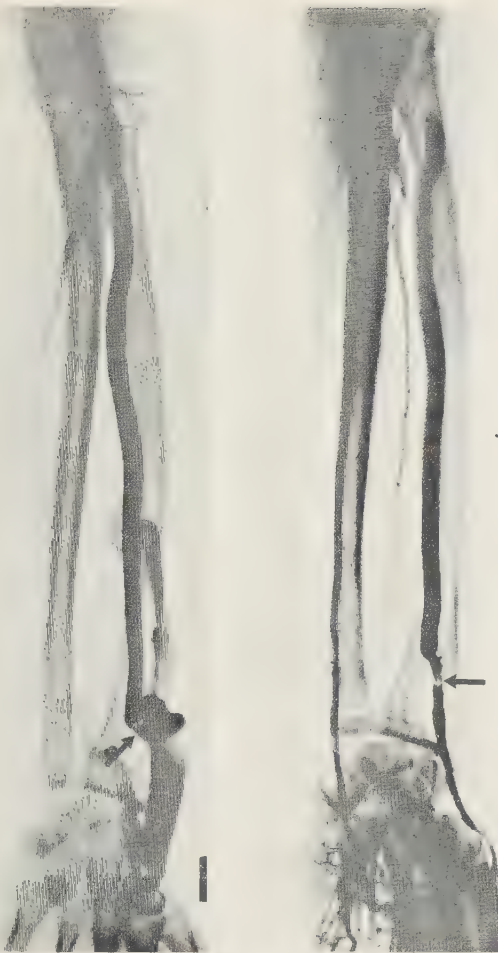


Fig. 30a. Gross dilation of the vein distal to the fistula (————→).

Fig. 30b. The vein is clotted and the fistula is closed. Because of this the radial artery gives blood flow to the arteries of the hand.

found in our material. Retrograde flow in the artery distal to the fistula is a regular finding in large traumatic arteriovenous fistulae. This retrograde flow is demonstrated in some cases of side-to-side anastomosis. In other cases the artery was not filled distal to the anastomosis which could be due to occlusion but is more probably an indicator of retrograde flow.

The arteriovenous fistula is an effective stimulator for development of arterial collaterals (Reid 1925) as demonstrated in (Fig 22).

Dilation of the vein leading from the fistula has also

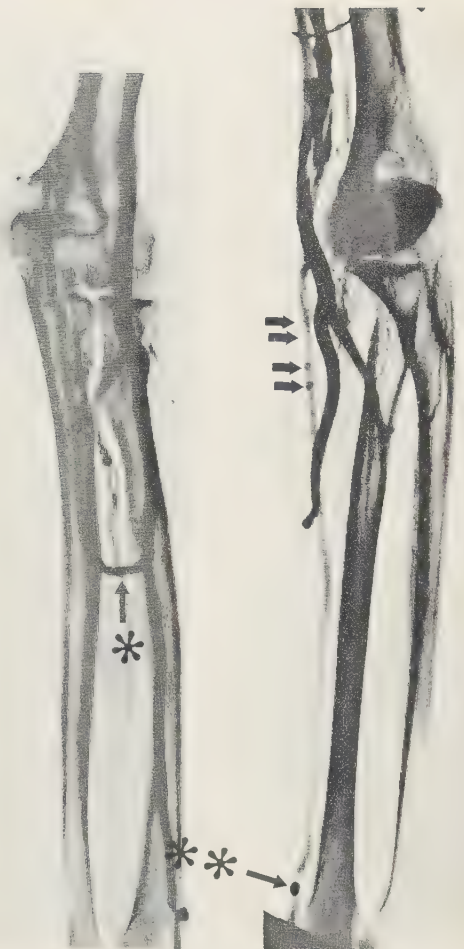


Fig. 30c and 30d. Bridge graft using the saphenous vein is anastomosed side-to-end from the radial artery (* ———→) to a vein just above the elbow. Small aneurysms at the site of multiple punctures of the graft (————→). Small aneurysms also at the site of the previous fistula (* * ———→). C: Volar dorsal. D: lateral view.

been a constant finding in patients with a well functioning fistula. In most cases several subcutaneous veins of the forearm became dilated and this is particularly advantageous in patients in whom the fistula has been created to allow for more puncture sites for intravenous therapy. In other cases only one main venous channel was present. This is the rule in patients with end-to-end or side-to-end anastomosis.

In anatomical and roentgenological literature no reports about the presence and function of communi-

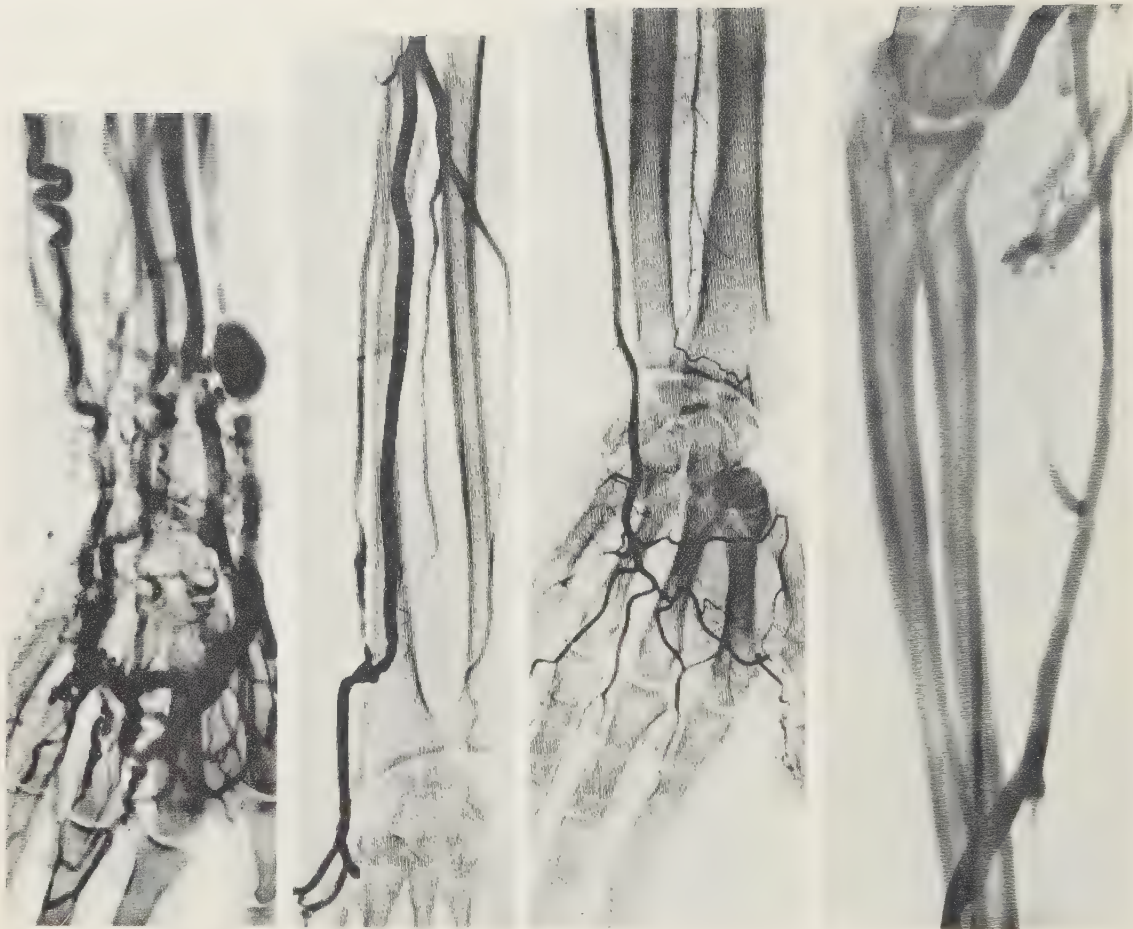


Fig. 31. General dilation of vessels, considerable local venous dilation close to the fistula and extensive net of arterial and venous collaterals.

Fig. 32. Incompetence of the valves in the distal veins. Concentration of contrast medium in the proximal part of the artery and the distal part of the vein approximately equal indicating main venous flow retrograde towards the hand.

cating veins between the deep and superficial venous systems in the forearm were found. It is well known that the main venous draining system on the forearm is the superficial. It is also known that muscular exercise during venous compression results in increased filling of the subcutaneous veins in the arm. In the leg, where the communicating veins have valves permitting flow only from the superficial to the deep

Fig. 33. Preoperative angiography. The radial artery is occluded after previous Quinton-Scribner shunts. Main arterial supply to the hand over the ulnar artery.

Fig. 34. Normal phlebogram in a healthy control performed with 50 mm Hg venous compression of the upper arm. No deep veins are filled in the distal part of the arm.

system, the superficial veins are emptied under these conditions. In our studies, no passage of contrast medium from the superficial to the deep veins in the forearm could be demonstrated. This finding gives further support to the opinion that in the lower arm communicating veins normally allow blood flow from the deep to the superficial venous system but not in the opposite direction.

HAEMODYNAMIC STUDIES IN PATIENTS WITH CIMINO-BRESCIA ARTERIOVENOUS FISTULAE

By Eric Lindstedt and Ivar Nordenfelt

The essential feature of a fistulous circuit is its low haemodynamic resistance. The systemic arterial pressure will therefore tend to decrease unless the low resistance is compensated for by increased resistance in other regions or elevation of the cardiac output. The latter of these two compensatory mechanisms seems to be the most important. The systemic arterial blood pressure will thus usually be within normal limits. This seems also to be the case with the heart rate, implying that the cardiac output is primarily caused by an elevation of the stroke volume (Binak et al. 1960). The cardiac output is thus elevated in many cases of chronic fistulae (Binak et al. 1960; Cohen et al. 1948; Muenster et al. 1959; Samet et al. 1964; Spurny & Pierce 1961; Warren et al. 1951 a). The cardiac output will then be equal to the sum of the normal cardiac output and the fistula flow (Sumner, 1969). Compensation for the fistula flow is complete when the flow does not exceed 40% of the cardiac output (Leslie et al. 1960).

It seems thus essential to know the size of the fistula flow when discussing the central haemodynamic effects caused by arteriovenous fistulae. We have tried to measure the fistula flow by using venous occlusion plethysmography of the forearm with the Cimino-Brescia fistula. Due to the very rapid filling of the venous system of the segment in the plethysmograph (within one or two heart beats) the recordings have been very difficult to evaluate and no completely satisfactory results have been obtained. Estimations of the shunt flows with this method have given values of 150–500 ml/min (Lindstedt et al. 1967). Measurements of the fistula flow during the operation of Cimino-Brescia fistulae have been made with an electromagnetic flow meter. As the incision in the skin has been kept as small as possible (2–3 cm), it has been difficult to place the probes on the artery proximally and distally to the fistula without stretching and kinking the vessel and thus interfering with the flow. Neither with this method, which also makes only

single measurements possible, have thus reliable results been obtained.

One of the first patients with Cimino-Brescia fistula at this hospital got pulmonary edema as a result of an intravenous infusion (Lindstedt et al. 1967). In this patient the fistula flow was studied by determination of the cardiac output with and without digital compression of the fistula and as no definite haemodynamic changes were observed, the pulmonary edema was attributed to overhydration in combination with heart disease. This made us, however, more observant of the possible risk of chronic arteriovenous fistula and therefore the present investigation was made.

Like many other investigators (for ref. see page 9) we have thus tried to estimate the fistula flow by measuring the cardiac output before and after occlusion of the fistula by digital compression. As the cardiac output rapidly adjusts to the new haemodynamic situation after closure of the fistula (Sumner, 1969) repeated observations have been possible. The patients selected for the study were those where the fistula flow was considered to be large at the clinical examination, showing signs of marked dilation of the draining veins and high intensity of the murmur and thrill of the fistula. The heart rate and arterial pressure and in a few cases central venous pressure and blood volume have also been recorded. In some of the patients P_{O_2} in the artery, and P_{O_2} and blood pressure in the draining vein at various distances from the fistula have been measured.

Methods

The haemodynamic studies were carried out on 10 patients, 14–73 years old, mean 51 years. Two of these were women, 14 and 43 years old (Table IV). In none of the patients was there evidence of cardiac decompensation at the time of the examination. The diagnoses of the patients are also given in Table IV.

Two polyethylene catheters were inserted percutaneously as described by Bernéus et al. (1954), one

TABLE IV. *Haemodynamic observations during open and closed Cimino-Brescia fistula.*

Pat.	Sex	Age	Diagnosis	Duration of fistula (months)	Open fistula					Central venous pressure (mm Hg)	Peripheral resistance (units)	
					Heart rate (beats/min)	Stroke volume (ml)	Cardiac output (l/min)	Arterial pressure mm Hg				
								S	D			M
B.P.	F	14	Uraemia	6	85	79	6.7	131	68	94	— 1	14.2
D.B.	F	43	Ca pancr.	3	75	87	6.5	107		82	—	12.6
B.H.	M	22	Uraemia	2 1/2	107	99	10.6	151	87	112	—	10.6
K.E.	M	49	Ca prost.	4	92	76	7.0	174	90	120	—	17.1
R.K.	M	50	Ca prost.	6	74	97	7.2	123	75	95	6	12.4
J.V.	M	57	Ca prost.	4	73	84	6.1	142	75	95	3	15.1
M.B.	M	58	Uraemia	2 1/2	79	95	7.5	163	90	120	4	15.5
H.H.	M	68	Ca prost.	2	57	132	7.5	112	60	83	—	11.1
A.N.	M	69	Ca prost.	5	74	115	8.5	184	82	120	6	13.4
M.S.	M	73	Ca prost.	1 1/2	69	88	6.1	120	50	79	—	13.0
Mean ± SD					79 ± 13.6	95 ± 17.1	7.4 ± 1.3	140 ± 26.6	74 ± 13.5	100 ± 16.6	4 ± 2.8	13.5 ± 2.0
Mean change ± S.E.M. Significance												

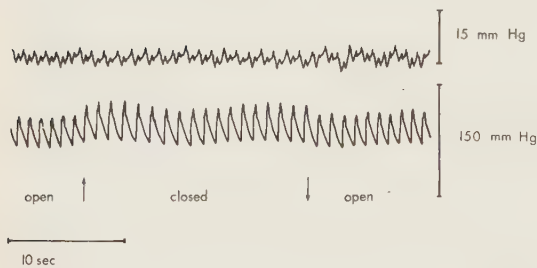


Fig. 35. Upper tracing: central venous pressure. Lower tracing: pressure in brachial artery of non-fistula arm. Recordings during open and closed Cimino-Brescia fistula. Note the insignificant changes in the central venous pressure and the rapid adjustment of the arterial pressure to the new level, when the fistula is closed or opened.

of these into the brachial artery, in most cases in the non-fistula arm, and the other into a vein draining the fistula. This vein was punctured 3–5 cm proximally to the fistula and in some cases the tip of the catheter was advanced to a site in the superior caval vein close to the right atrium.

Arterial and venous blood pressures were measured by inductance manometers and recorded on a direct writing electrocardiograph (Elema 81). Mean arterial pressure was obtained by electrical integration. Heart

rate was monitored from ECG recordings. Measurement of cardiac output was made with dye-dilution technique with bromsulphalein as indicator (Wassén 1956). Peripheral resistance was calculated as the quotient of the mean arterial pressure in mmHg (minus central venous pressure, when this was measured) and the cardiac output in l/min and expressed in arbitrary units.

The patients rested for at least 30 minutes before the cardiac output measurements started. The first determination of cardiac output was made with the fistula open, the second after 3 minutes of digital compression of the fistula, the third after the fistula had been open again for 3 minutes, the fourth after another 3 minutes of compression, and in some cases a fifth measurement was made after the fistula had been open again for 3 minutes. In Tables IV and V the mean values of these measurements for open and closed fistulae are given.

In five of the patients plasma volume was measured using T 1824 (Evans blue, 30 mg) or RIHSA (¹³¹I or ¹²⁵I, 2–4 µCi) as an indicator. Blood samples were obtained at 10, 20 and 30 minutes after the injection and the concentration at zero time was calculated by

Heart rate (beats/min)	Stroke volume (ml)	Cardiac output (l/min)	Closed fistula			Central venous pressure (mm Hg)	Peripheral resistance (units)	Fistula flow (l/min)	% of cardiac output during open fistula
			Arterial pressure mm Hg						
			S	D	M				
81	78	6.3	130	73	98	— 1	15.7	0.4	6.0
74	85	6.3	111	70	89	—	14.1	0.2	3.1
103	94	9.7	157	93	120	—	12.4	0.9	9.1
91	76	6.9	178	94	128	—	18.6	0.1	1.4
63	106	6.7	131	81	102	1	15.1	0.5	6.9
69	68	4.7	150	79	105	1	22.1	1.4	23.0
78	87	6.8	167	91	127	4	18.1	0.7	9.3
54	130	7.0	117	65	84	—	12.0	0.5	6.7
74	107	7.9	203	93	134	3	16.6	0.6	7.1
69	86	5.9	125	54	85	—	14.4	0.2	3.3
76 ± 13.9	92 ± 18.2	6.8 ± 1.3	146 ± 29.5	79 ± 13.8	107 ± 18.8	2 ± 1.9	15.9 ± 3.1	0.6 ± 0.4	7.6 ± 6.0
— 2.9 ± 1.0	— 3.5 ± 2.1	— 0.6 ± 0.1	6.2 ± 1.6	5.1 ± 0.8	7.2 ± 1.1	— 2.0 ± 0.9	2.4 ± 0.6		
p < 0.025	N.S.	p < 0.005	p < 0.005	p < 0.001	p < 0.001	N.S.	p < 0.005		

extrapolation of the disappearance curve plotted semilogarithmically. In some of the cases the plasma volume was obtained from a single 10-minute value as suggested by Gregersen (1944). The total blood volume was calculated by multiplying the haematocrit by 0.91 to obtain "whole body haematocrit" (cf. Gregersen & Rawson 1959).

P_O₂ was determined in blood samples drawn simultaneously from the artery and the vein. The measurements were carried out on an Eschweiler Comb-Analysator U.

Results

The main purpose of the present investigation was to analyse the central haemodynamics during open and closed Cimino-Brescia fistulae. The rapid adjustment (Sumner 1969) of the cardiovascular dynamics after closure of the fistula was verified. After digital compression of the fistula the heart rate and arterial pressure stabilized on the new level within seconds (Fig 35). This made it possible to determine the cardiac output repeatedly under relative steady state conditions with open as well as closed fistula.

The cardiac output was higher in all cases when the fistula was open, and the difference between the

values during open and closed fistula can be considered a rough estimate of the fistula flow. This difference probably represents a minimum value of the fistula flow as it cannot be excluded that there is some decrease of the flow to other tissues when the fistula is opened.

The mean fistula flow was found to be 0.6 l/min (7.6% of cardiac output, Table IV). Only in one patient (J.V.) the fistula flow exceeded 1 l/min (1.4 l/min, 23%). Subsequent studies in this patient, four and eleven months later, showed however, that the fistula flow gradually decreased (Table V). Clinical examinations of another patient (R.K. Table V) indicated increase of the fistula flow which was confirmed by an investigation seven months later. After reconstruction the fistula showed a lower flow another six months later, but a fourth examination one and a half year later showed again the same, high fistula flow.

The heart rate decreased in all but one case when the fistula was closed and this decrease was significant (cf Cohen et al. 1948). The stroke volume decreased in eight of the ten patients with the fistula closed but the mean change was not significant. The significantly larger cardiac output when the fistula is

TABLE V. *Repeated haemodynamic studies in two patients during open and closed Cimino-Brescia fistula.*

Pat.	Sex	Age	Open fistula								
			Duration of fistula (months)	Heart rate (beats/min)	Stroke volume (ml)	Cardiac output (l/min)	Arterial pressure mm Hg			Central venous pressure (mm Hg)	Periphera resistance (units)
							S	D	M		
J. V.	M	57	4	73	84	6.1	142	75	95	3	15.1
		58	8	64	89	5.7	117	62	87	1	15.1
		58	15	58	110	6.4	122	53	82	—	12.8
R. K.	M	50	6	74	97	7.2	123	75	95	6	12.4
		50	13	87	107	9.3	123	74	97	8	9.6
		51	19	70	107	7.5	127	75	100	6	12.5
		52	36	81	140	11.3	144	77	104	—	9.2

open is thus not primarily caused by an increase of stroke volume: the increase in heart rate contributes to about the same degree.

The arterial pressure as well as the total systemic resistance rose significantly after closure of the fistula. Central venous pressure was only measured in five of the patients and it decreased in three of them when the fistula was closed. Even with open fistula the central venous pressures were essentially within normal limits.

Blood volume was determined in five patients and twice in two of them (Table VI). In only one of these patients (H.H.) the total blood volume and plasma volume were found to be higher than normal, in spite of the fact that the estimated fistula flow was not especially large (0.5 l/min). The measurement of the fistula flow was made about one month earlier but there was no clinical impression of increase of the flow during this time. Three days after surgical closure of the fistula in this patient the blood volume was unchanged.

Table VII shows P_{O_2} of the artery as well as P_{O_2} and pressure in the draining veins at different distances from the fistula. It can be seen that in the few cases studied the venous P_{O_2} equals the arterial P_{O_2} as high up as in the axilla (35–45 cm from the fistula). At the level of the elbow (20–30 cm) the venous P_{O_2} was very similar to the arterial P_{O_2} except in one patient. At a later examination this patient showed, however, a P_{O_2} at a level which was very close to the arterial P_{O_2} . The venous pressure was surprisingly low even close (5–8 cm) to the fistula, the highest

pressure being 16 mmHg. There seems to be no correlation between the pressure and the fistula flow. In one patient the fall of the mean arterial pressure from a central artery down to an arterial site just before the fistula was determined and was found to be 22 mm Hg, while the pressure gradient over the fistula itself was 45 mm Hg.

Discussion

When deliberately creating an arteriovenous fistula in a patient one must keep in mind the potential risk of eventually causing cardiac decompensation. That this risk should be high is contradicted by the fact that none of the about 200 patients with Cimino-Brescia fistulae at this hospital has developed obvious heart failure attributable to the shunt during an observation period of up to five years. Only one patient now studied, mentioned below, showed significant increase in heart size. In some of the uraemic patients, who underwent dialysis, small variations in heart size were noted, probably due to changes in the degree of hydration.

The present study was, however, undertaken, as it was thought of great interest to investigate the haemodynamic consequences of the fistula, to make it easier to evaluate the strain placed on the circulation. It should be pointed out that the patients selected for this study were those where the fistula flow was suspected to be large. Muenster et al. (1959) have provided evidence that heart failure may be elicited in the apparently healthy heart by the circulatory load

Heart rate	Stroke volume	Cardiac output	Closed fistula			Central venous pressure (mm Hg)	Peripheral resistance (units)	Fistula flow (l/min)	% of cardiac output during open fistula
			Arterial pressure mm Hg						
			S	D	M				
59	68	4.7	150	79	105	1	22.1	1.4	23.0
52	77	4.8	121	67	89	0	18.5	0.9	15.8
54	109	5.9	146	67	100	-	17.0	0.5	7.8
53	106	6.7	131	81	102	1	15.1	0.5	6.9
81	94	7.6	130	82	101	2	13.0	1.7	18.3
55	105	6.8	135	76	103	3	14.7	0.7	9.3
77	123	9.5	144	76	102		10.7	1.8	15.9

put upon the heart. Many of the patients in this study were old, implying that the condition of the heart might not be the best. In some of the patients an extra demand was imposed on the heart by arterial hypertension or anaemia, e.g. one patient (R.K., duration of fistula 36 months, Tables V and VI) had a cardiac output of 9.5 l/min (closed fistula) probably due to severe anaemia (6.5 g/100 ml). Parallel with the development of the anaemia in this patient and the deterioration of his condition due to the malignant disease, the heart size increased to 1,230 ml (650 ml/m²). He showed, however, no other signs of heart failure. As earlier stated no evidence of cardiac decompensation was found in any of the other patients at the time of the study or later and the heart size was within normal

limits in all cases except the one mentioned. The cardiac output after closure of the fistula was also normal in all patients, except possibly in one patient (J.U.) the one who had the largest estimated fistula flow, 1.4 l/min or 23% of the cardiac output. Subsequent studies during 11 months in this patient showed, however, that the fistula flow gradually diminished.

In one patient (R.K.) clinical examination gave the impression of a gradual increase of the fistula flow and this was confirmed by an investigation seven months later. Reconstruction of the fistula caused the flow to decrease but when it was studied one and a half year later the flow was again elevated.

TABLE VI. Blood volume and haemoglobin values in patients with Cimino-Brescia fistulae.

Pat.	Sex	Age	Duration of fistula (months)	Total blood vol. (l)	Total blood vol. (ml/kg)	Plasma volume (l)	Plasma volume (ml/kg)	Red cell vol. (l)	Hcr (%)	Hb (g/100 ml)	Total Hb amount (g)	Total Hb (g/kg)	Fist. flow (l/min)	% of C.O. (open fist.)
B.P.	F	14	6	2.5	89	1.9	68	0.6	26	9.0	208	7.4	0.4	6.0
D.B.	F	43	3	5.5	75	3.6	49	1.9	38	12.3	618	8.5	0.2	3.1
R.K.	M	50	13	5.7	66	3.8	44	1.9	37	12.4	645	7.4	1.7	18.3
		52	36	5.7	62	4.6	62	1.1	21	6.5	339	4.5	1.8	15.9
J.V.	M	58	8	4.6	61	2.9	39	1.7	41	13.6	572	7.6	0.9	15.8
H.H.	M	68	3	6.9	103	5.1	76	1.9	30	9.6	605	9.0	0.5*	6.7
		68	**	6.7	100	4.9	73	1.8	30	9.7	591	8.8	0	0

*measured 37 days earlier

**three days after closure of the fistula

TABLE VII. P_{O_2} of the artery and P_{O_2} and pressures in the draining veins at different distances from the Cimino-Brescia fistula.

Pat.	Sex	Age	Duration of fistula (months)	Fistula flow (l/min)	Arterial P _O ₂ (mm Hg)	Venous P _O ₂ (mm Hg) Distance from fistula (cm)			Venous pressure (mm Hg) Distance from fistula (cm)		
						35 45	20 - 30	5 8	35 45	20 - 30	5 - 8
B.P.	F	14	6	0.4	92 99		94	91		1	7
K.E.	M	49	4	0.1	78 96	80	83	79	7	8	10
R.K.	M	50	6	0.5	80 84	81			6	8	16
		50	13	1.7	89 90		84	89		13	15
		51	19	0.7	86 92	85	96	92	5	5	7
J.V.	M	57	4	1.4	78 80		46	77	—		6
		58	8	0.9	79 83		78	82		4	8
		58	15	0.5					6	5	5
A.N.	M	69	5	0.6	71 74	74	73		8	11	

The estimations of the fistula flow have in this study been based on the assumption that the flow to the tissues of the body is unchanged whether the fistula is closed or not. The shunt-flow will then be equal to the difference between the cardiac output with open and with closed fistula. Experimental studies on chronic fistulae in dogs by Leslie et al. (1960) support this assumption.

The elevation of the cardiac output does not, however, completely compensate for the falling blood pressure when the low-resistance circuit, the fistula, is switched in, as the mean pressure is then significantly lower. It can be calculated that another 0.5 l/min would be required (i.e. an increase from the measured 7.4 l/min to 7.9 l/min) to maintain a blood pressure at the level of the closed fistula. This might probably be explained by a resetting of the baroreceptors at this slightly lower pressure as the small extra increase of the cardiac output could easily be achieved, if necessary. Another way of maintaining the blood pressure would be to raise the peripheral resistance (excluding the fistula) but this would compromise the flow to the tissues. If the above mentioned assumption is correct that the flow to all tissues of the body is unchanged when the fistula is open, the resistance in these regions must in fact be lowered as the mean pressure has decreased. As it is not known if such a vasodilation actually takes place, it is possible that the flow to the rest of the body decreases when the fistula is open, and the measurements in the present investigation will in that case consequently somewhat underestimate the fistula flows.

The compensatory elevation of the cardiac output

caused by the fistula has in this investigation probably been produced both by an increase in the heart rate and stroke volume. Even in the patients with large fistula flows the central venous pressure was essentially within normal limits.

The total blood volume and plasma volume of the few patients studied were normal except in one patient (H.H.) where the values were elevated for some unknown reason, as the fistula flow in this patient was not especially large and the blood volume remained elevated after closure of the fistula. In a study by Warren et al. (1951 b), in general the patients with increased blood volume were those with clinical evidence of a functionally large fistula.

The measurements of P_{O_2} in the veins draining the fistula revealed that the P_{O_2} approximated the arterial values as high up as in the level of the axilla in some of the cases. Closer to the fistula samples for determination of arterial P_{O_2} can definitely be taken from the draining veins.

From the pressure measurements in the veins draining the fistula it can be concluded that the pressure fall over the artery leading to the fistula (due to the high flow) and the fistula itself is rather large, as the pressure close to the fistula usually is of the order 5–15 mmHg and never exceeds 20 mmHg.

In conclusion it can be stated that the blood flow shunted through a Cimino-Brescia fistula is usually rather low (mean 0.6 l/min and 7.6% of the cardiac output) and seldom exceeds 1 l/min. The circulatory load placed on the heart by this flow is thus small and has not in any case led to obvious cardiac decompensation.

ADDUCTOR POLLICIS MUSCLE BLOOD FLOW IN PATIENTS WITH CIMINO-BRESCIA ARTERIOVENOUS FISTULAE

The Cimino-Brescia arteriovenous fistula might lead to decreased perfusion pressure and decreased nutrition to the tissues of the arm. To investigate this possibility we measured the blood flow to the adductor pollicis muscle in the arm carrying the fistula compared to the normal arm using the ^{133}Xe clearance method described by Lassen et al. (1964).

Clearance of ^{133}Xe injected intramuscularly is now a well established technique for the evaluation of blood flow in patients with occlusive vascular disease. Lassen et al. (1965) found that there was good correlation between the values obtained with this technique and with venous occlusion plethysmography. The xenon technique has many advantages: it is simple and of very little discomfort to the patient. It has some disadvantages: the trauma of the injection might affect the elimination of the isotope and it is of great importance to make the injection slowly and carefully and to avoid leakage of the solution into the subcutaneous tissues.

Methods

^{133}Xe dissolved in sterile saline solution (0.15 M sodium chloride) was obtained from the Radiochemical Centre, Amersham, England. The solution contained about 1 mCi per ml and 0.05–0.1 ml was injected slowly into the adductor pollicis muscle of each hand using a fine needle and carefully avoiding the injection of air bubbles. The needle was slowly withdrawn half a minute after the end of the injection.

The disappearance rate of the isotope was measured with two sodium iodide crystals coupled to a logarithmic ratemeter with a time constant of three seconds. Each crystal was placed about 10 cm from the skin and the collimator was adjusted to record from an area 10 cm in diameter.

Resting clearance was measured during three minutes. A pneumatic cuff placed on each arm above the elbow was then rapidly inflated to a pressure of 270 mm Hg. The nondisappearance of isotope was checked for half a minute and the patient was then

asked to open and close his fists including the thumbs as forcefully as possible. After 1 1/2–2 1/2 minutes, exercise was no longer possible due to ischaemic pain. The occlusion was maintained for a period of 3–4 1/2 minutes and then was suddenly released. The clearance of isotope was followed during the period of reactive hyperaemia, and the steepest part of the curve used for calculation of maximal blood flow.

Calculations

The muscle blood flow was expressed in ml per 100 ml of tissue per minute. Complete diffusion equilibrium is assumed and the Fick principle is applied to the tissue area studied. The partition coefficient, λ , between muscle and blood is known to vary with the haematocrit value. It was calculated by Conn (1961) to be 0.70 for a haematocrit of 40. This value was used even for patients with anaemia. That might have included a slight error but the difference between the two thumbs would not be affected by this error.

The calculation was made using the formula described by Lassen et al. (1964).

Results

Thirteen patients were studied in whom the fistula was regarded to be particularly large because of dilated veins and a strong thrill palpable over the fistula. All patients had side-to-side anastomoses between the radial artery and the cephalic vein. The resting blood flow and maximal blood flow of the two sides are listed in Table VIII. The values given are usually means of duplicate values and refer to ml per 100 ml of tissue.

The resting flow was within normal limits without significant difference between sides. All patients responded to ischaemic exercise with a considerable increase in muscle blood flow. The increased flow started immediately after release of arterial compression (Fig. 36). The increase in blood flow was, in most of the patients, of short duration. There was

TABLE VIII. Adductor pollicis muscle blood flow estimated from ¹³³Xenon wash-out curves at rest and after ischaemic exercise. (Maximal blood flow)

Patient	Sex, age	Time after creation of fistula (months)	Resting flow		Maximal flow	
			Normal side	Fistula side	Normal side	Fistula side
BJ	M 71	2	4.0	2.4	77	82
EF	M 68	3	7.2	4.8	24	82
EN	M 70	4	2.4	2.4	82	56
ES	M 86	5	9.0	2.0	89	38
EL	F 48	6	2.8	4.4	40	79
PS	M 34	7	4.0	4.4	66	67
KL	M 64	8	1.6	7.2	30	47
HJ	M 70	12	2.4	3.6	48	42
LEH	M 21	21	7.3	3.2	55	77
JV	M 59	21	3.2	2.0	28	136
RK	M 51	23	8.6	5.1	63	38
AL	M 24	29	4.0	3.2	63	70
BH	M 24	31	4.0	4.0	27	26
Mean value			4.7 ± 0.69	3.7 ± 0.41	53 ± 6.2	65 ± 8.0
± S.E.M.						
Mean difference				0.9 ± 0.85		11 ± 11.2
± S.E.M.						
			Not significant		Not significant	
Excluding patient JV who had exceptional values:				Mean value	55 ± 6.3	59 ± 5.8
				± S.E.M.		
				Mean difference	3.3 ± 8.5	
				± S.E.M.		Not significant

some variation in the values on the two sides, but no significant difference between sides was measured. One patient, J.V., had exceptional values with a considerably higher flow measured on the fistula side. This might be due to technical error but no satisfactory explanation can be given.

No difference between sides was noted in regard to the length of time the patient could continue his ischaemic work.

No patients reported subjective symptoms of claudication, nor did they have objective signs of decreased blood flow such as dyspilation, nail changes, or ulcerations. A few patients reported that their fingertips on the fistula side felt colder than those of the normal hand if they were outdoors in cold weather without wearing gloves. No patients reported a decrease in their ability to perform moderate or, in some cases, even hard manual labour.

Discussion

Large congenital or acquired arterio-venous fistulae can lead to a steal of blood from the nutritive flow of the tissues distal to the fistula, resulting in claudication and ulceration.

Studies of resting muscular and subcutaneous blood flow in patients with Cimino-Brescia arteriovenous fistulae was reported by Lazorthes (1969). No significant differences could be demonstrated between sides. The skin circulation is, however, very dependent on the skin temperature. The increased flow through the subcutaneous veins of the arm carrying the fistula gives increased temperature in the skin overlying the veins which can easily be demonstrated by palpation and by thermographic photography (Lindstedt 1970) The resting blood flow to muscle tissue is also of little interest as this can be entirely normal in patients with severe arterial insufficiency.

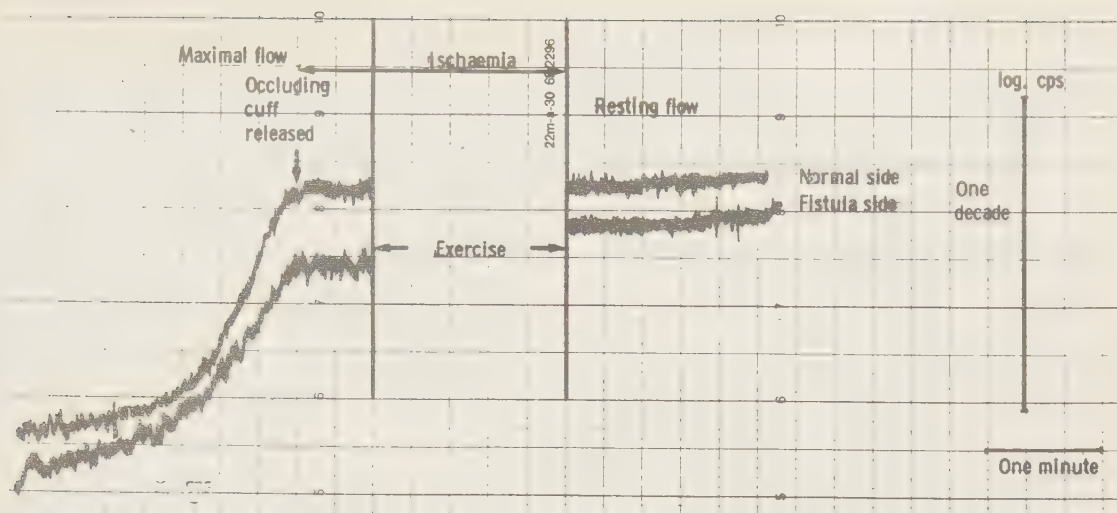


Fig. 36. REGISTRATION OF RADIOACTIVITY FROM $^{133}\text{XENON}$ INJECTED INTO THE ADDUCTOR POL-LICIS MUSCLE.

Read from right to left. Resting flow equal on both sides. Note immediate start of maximal blood flow after release of occlusion. Maximal flow slightly greater on normal side.

The subjective sensation of cold fingers reported by a few patients might indicate a decrease in skin blood flow but it has in these patients been of little practical importance. No objective studies of the skin circulation have been made in our patients.

All of the patients studied could respond to ischaemic exercise with an increase in muscular blood flow. The increase in flow started immediately after release of tourniquets and the decreased response, typical for patients with claudication due to arteriosclerosis in

the leg, was never recorded. There is great variation in the maximal flow values in different patients. The intensity of exercise during ischaemia seems to be important in interpreting the results. No attempts to standardize the exercise have been done, as the fistula has been created in the nondominant forearm if suitable vessels were available. It is concluded that the study has shown no indication of decreased muscle blood — flow in the hand which can be ascribed to presence of a Cimino-Brescia fistula.

OTHER POSSIBLE COMPLICATIONS OF THE CIMINO-BRESCIA FISTULA

Besides general and local circulatory effects an arteriovenous fistula can cause several types of complications. Our patients with Cimino-Brescia fistulae have been observed concerning eventual signs of some of these complications.

ON "HYPERTROPHY" OF THE LIMB CARRYING THE FISTULA

The so-called hypertrophy observed in patients with congenital arteriovenous fistulae and traumatic fistulae occurring before the epiphyses are closed is mainly caused by oedema and by dilation of the veins. Real skeletal overgrowth with increase in length and thickening of the corticalis of the long bones is also found. The cause for these skeletal changes is not fully understood. Increased blood flow and flow rate may give a rise of temperature of the growth plates. Increased venous pressure and increased venous oxygen tension may also play a part. Induction of venous stasis has been reported to stimulate skeletal growth (Helferich 1887; Bier 1903; Hutchison & Burdeaux 1954). Studies of skeletal growth have not been reported in patients having Cimino-Brescia fistulae, but the fear of skeletal changes has been an argument for avoiding this type of fistula for haemodialysis in children (Roberts & van Zyl 1968; Cameron 1970).

In the present series of patients only three were definitely below the age for closure of the epiphyses. In these patients, 13, 14 and 7 years of age, roentgen examinations of their forearms were made 15, 25 and 10 months after induction of the fistula. Standard films were made and the length of the radius and ulna were measured from the tip of the olecranon to the styloid processes. The thickness of the cortices was measured on corresponding points. No differences could be measured between sides.

These data do not support the contention that skeletal overgrowth occurs in children with subcutaneous arteriovenous fistulae of this type.

MORPHOLOGICAL CHANGES OF THE VESSELS INVOLVED

The morphological changes known to occur secondary to congenital and acquired arteriovenous fistulae include dilation of the artery and vein. Absolute increase of the median coat of the artery is reported by Ingebrigtsen (1965) but a decrease in thickness of the arterial wall is often encountered (Reid 1925, Petrovsky & Milonov 1967). In the vein, thickening of the wall is a constant finding.

Dilation of the vein is clinically obvious in all our patients having Cimino-Brescia fistulae even if there is great variation as to degree. The wall of the vein leading from the fistula is palpably thicker than normal. The wall thickening was verified at autopsy in three cases and in biopsy specimens taken from patients at operation with closing of the fistula. (Department of Pathology, Dr Joachim Mark). The histological findings did not differ from what was reported by Petrovsky & Milonov (1967) in experimental fistulae, by Glashan & Walker (1968) in Quinton-Scribner shunts and by Lazorthes (1969) in Cimino-Brescia fistulae. The changes are characterized as "arterialization" with an increase of muscle and connective tissue in the median coat and splitting of the elastic fibres.

Aneurysmal dilation of the vein in the region of the fistula leading to skin necrosis and impending rupture of the vein was described by Röhl et al. (1968). In two of our patients, an aneurysmal dilatation of the vein could be seen and was also demonstrated by angiography (see above) but no tendency for the sac to increase with time nor to rupture or to cause skin ulceration was present. Avoiding too complete stripping of the adventitia in dissecting the vein probably minimizes the risk for this complication.

Our angiographic studies have shown dilation of the artery to be a constant finding in patients with well functioning fistulae. The aneurysmal degeneration of the arterial wall reported as a complication in long-standing traumatic arteriovenous fistulae (Voll-

mar 1964, and others) has not been found in our patients. In a few cases where the artery was studied microscopically, very small changes were noted.

SEPTICAEMIA

Septicaemia has been reported to arise from mycotic vegetations in abnormal arteriovenous communications (Parmley et al. 1954). In many of these cases both endarteritis and endocarditis are present. Dogs with large arteriovenous fistulae frequently developed endocarditis (Lillehei et al. 1950). Local infections and septicaemia are common in patients with Quinton-Scribner teflon-silastic arteriovenous shunts, probably due to the penetrations through the skin. Infections have apparently been uncommon in patients with subcutaneous arteriovenous fistulae in spite of the repeated cannulations of the veins with large bore needles. Endocarditis was reported as the cause of death in one of the original cases published by Brescia et al. (1966) and one case most probably representing endarteritis with *Staphylococcus* septicaemia was reported by Smith et al. (1969). In this case the patient recovered following the treatment with penicillin.

Mignon et al. (1969) reported a patient with thrombotic vegetations at the fistula containing *Moraxella* bacilli resulting in septicaemia. Cure was achieved after excision of the fistula region. Seven cases of septicaemia in six patients with two attacks of pulmonary embolism (Levi et al. 1970) with growth of *Staphylococcus aureus* or *Pseudomonas* led the authors to use better sterile precautions during dialysis and thereafter no more cases of septicaemia occurred in their unit.

In the present series, no periods of fever suggesting endocarditis or local symptoms of endarteritis have occurred. In one patient, however, an infected haematoma occurred at the site of puncture for haemodialysis. She died with septicaemia. At autopsy the infected haematoma was found to communicate with the arterialized vein and *Staphylococcus aureus* was grown from the haematoma. In a second case a similar infected haematoma occurred after dialysis, in this patient early operation was performed with ligation of the vein and a new fistula was made at another site. She recovered uneventfully without signs of septicaemia.

GENERAL DISCUSSION

For patients on chronic haemodialysis using Quinton-Scribner shunts, complications related to the shunts such as bleeding, clotting, skin necrosis, infection etc., are the main reason for hospitalization and the need of acute intervention by the doctor in charge. After Brescia et al. (1966) had reported the construction of arteriovenous fistulae and venipuncture for haemodialysis, hopes arose that the disadvantages of the external shunts would be eliminated. We now have five years of experience with the Cimino-Brescia type of arteriovenous fistula and all our patients on maintenance dialysis have this fistula. In many dialysis centers the external shunt is still used, including several centers in Sweden. The main objections to the Cimino-Brescia fistula have been that the construction of a fistula is technically difficult, that the nursing staff have difficulties handling it, that the blood flow to the dialysis machine might be insufficient and that the fistula might affect the central and local circulation of the patient.

In our experience, the construction of a Cimino-Brescia arteriovenous fistula is relatively simple provided the patient has normal vessels. It is considerably more difficult, however, to use the fistula for dialysis, and our nursing staff had some difficulties during the first period. Now the nurses are very satisfied with the fistula technique and prefer the fistula to the external shunt.

The dialysis effect measured as decrease of creatinine and BUN, compared in some patients with external shunts to other patients with fistulae, was found to be about 10% lower with the fistula during the first half year of its use. When the investigation was repeated one year later, no significant difference could be measured (Lindstedt 1970).

Psychological studies in patients on maintenance dialysis have shown that they are quite concerned with the presence of an external shunt and the risk of complications from it (Malmquist 1969). If a subcutaneous fistula is used, many of these psychological problems disappear. In addition the patient is more mobile. He does not have to think about the fistula in his daily activities, he can bathe and exercise freely and does not have to be near hospital in order

to get early treatment in case of shunt complications. Nine of our patients have tried both external and internal shunts. Some of them were very reluctant to try an internal fistula when the external shunt clotted, but after the internal fistula was created none of them wanted to return to the external shunt.

For haemodialysis treatment in acute renal failure, the Quinton-Scribner shunt is still the standard method in our hospital parallel to percutaneous puncture of the femoral vein according to Seldinger (1953). Even in these patients arteriovenous fistulae would be a possible method, at least in patients with large subcutaneous veins in the arm.

The need of repeated venipuncture is a disadvantage in sensitive patients including children. In our experience, however, this has not been a significant problem. The technical skill of the nurses and the confidence of the patient are of great importance in this respect.

We previously thought that the fistula would be unsuitable for home dialysis (Lindholm et al. 1968). Shaldon et al. (1968) have, however, reported good experience with the fistula for home dialysis. In the last two years several of our patients on hospital dialysis have learned to cannulate their arterialized veins themselves, and one patient has started home dialysis with a fistula.

The Cimino-Brescia arteriovenous fistula has been found useful for other purpose. The rapid flow through the arterialized veins gives rapid dilution of an injected drug and the risk of thrombophlebitis after injection of locally irritating cytotoxic drugs is thus diminished. The vein can also be used for intravenous infusions and for obtaining blood samples. This is especially useful in patients who will undergo surgery where intravenous therapy is expected to be required for some time postoperatively.

The subcutaneous veins in the forearms of the fistula patients have been shown to contain oxygenated blood. This venous blood can be regarded as arterial blood for the determination of arterial PO_2 and PCO_2 and arterial puncture avoided. This can be of value after operations, especially kidney transplantation.

A patient should not be scheduled for kidney trans-

plantation without having a functioning arteriovenous fistula, even if haemodialysis is not required in the near future. Otherwise, there is the risk that his subcutaneous veins might be destroyed by blood sampling or injections before the operation or in the immediate postoperative period. Construction of an arteriovenous fistula might then be impossible and eventual haemodialysis difficult to perform. The Cimino-Brescia fistula is especially preferable to the external shunt in patients who will receive kidney transplants as the risk of septicaemia is reduced.

It is relatively easy to create a functioning fistula in a patient with uraemia. In the other two groups of patients, the frequency of primary function is much lower and the risk for secondary closure is rather high. This difference may depend on several factors. It has been shown that uraemia patients often have changes in their primary hemostasis and their coagulation and fibrinolytic systems. These changes would decrease the tendency for early thrombosis of a fistula. Other factors acting in the same direction are the low haematocrit and the low viscosity of the blood in uraemic patients. On the other hand many uraemic patients have an increase of some coagulation factors and the fibrinolytic activity of the blood is decreased. These changes could be the explanation for repeated clotting of fistulae in three of the dialysis patients. In one of these patients even the local fibrinolytic activity of the vein wall was low. Early clotting of the fistula after a successful kidney transplantation may be due to the normalization of the platelet adhesiveness after transplantation (Ljungqvist et al. 1969). Decrease of the plasminogen activators induced by large doses of corticosteroids (Larsson 1971) may be a contributory factor.

There has been some disagreement about the most suitable anastomosis technique for this type of arteriovenous fistula. We started to use the technique originally described by Brescia et al. (1966) with side to side anastomosis between the radial artery and the cephalic vein. The main reason was to save the artery if the fistula was no longer needed and our experiences have not given reason to change from this standard procedure. Variations of the surgical technique have been used in patients where the anatomical conditions make the side to side anastomosis unsuitable. In such cases, the anastomosis can be made end to end, or end to side. The number of patients with these types of anastomoses is small and no significant difference

in the patency of fistula can be found. Arteriovenous fistulae in the leg have not been performed as yet. We have some experience with the use of saphenous venous grafts with fair results in uraemic patients and bad results in non-uraemic patients. It must be kept in mind, however, that the operation was performed in patients where other attempts to create a fistula had failed.

The experience with the use of a fistula in three children and in some female adults with poor veins suggest that the fistula could be made and used without great difficulties in children down to about 10 years. It is possible that the fistula could be used even in smaller children, e.g. for intravenous therapy such as transfusions. On a nine month old baby, the fistula stayed open only a few days. In such patients an operating microscope might improve surgical results.

Even in patients with advanced arteriosclerosis of the radial and ulnar arterial wall the anastomosis could usually be made without difficulty. The condition of the vein, however, is critical. If the vein had been the site of a thrombophlebitis, long term function of the fistula could be achieved only in uraemic patients. The most suitable veins were found on the dorsal radial side of the wrist. In some patients these veins were, however, destroyed by previous puncture. The basilic vein on the ulnar side of the arm is less accessible for injections and is often preserved. It can be used for anastomosis to the ulnar artery. The small veins on the volar side of the wrist could allow the construction of an anastomosis but they are thinwalled and are easily kinked. Only in few cases it was possible to obtain permanent function of a fistula to one of those veins.

Murmurs are audible over the anastomosis shortly after the operation in many cases but not in all, presumably due to low flow through the fistula. It should, however, have appeared within 12 hours. Otherwise the fistula must be considered to have clotted. At reoperation this has always been seen. The murmur is much less obvious in end to end anastomosis.

If a transverse incision is used this can be small, 2–4 cm, and the subcutaneous dissection needed is minimal. This is advantageous in patients with a bleeding tendency. Good haemostasis is important but not always possible. It is then important to make loose skin sutures to allow for drainage and to avoid a subcutaneous haematoma which might compress the anastomosis. The bandage must also be loose or none at

all, even the slightest compression from a bandage could cause thrombosis of the fistula.

Anderson et al. (1970) and several other authors have pointed to the importance of saving the patients' subcutaneous veins, an unrecoverable natural resource. In some patients the lack of suitable veins makes lifesaving intravenous treatment difficult or impossible. Many doctors and nurses like to use the cephalic vein at the wrist for injections. I think that this vein should be avoided in the lower third of the arm. In patients where repeated venipuncture or long-time intravenous therapy is expected an arteriovenous fistula should be made early. The procedure is simple and reversible.

In some patients with poor veins the fistula function was not good enough to allow dialyses and a fistula was constructed in the other arm also. This gave more alternatives for venipuncture and the fistula veins had time to rest between dialyses, thus fistula function improved. In one patient, a Quinton-Scribner shunt was made in one arm, a fistula in the other and the external used in the beginning. When this shunt clotted the fistula had grown and the veins were dilated enough to allow good use. This is a procedure used by others (Goldsmith et al. 1970). Preferable to this is the construction of the fistula some time before dialysis is required especially if the patient has small veins.

In cases of poor fistula function, brachial arteriography has been shown to be a simple and valuable examination. It can demonstrate whether the reason for poor function is a poor anastomosis or local conditions in the vessels themselves. Angiography is also valuable in the study of the arterial side to find a suitable place for a new anastomosis in cases where previous arteriovenous shunts or fistulae have failed.

Phlebography is useful for demonstration of stenotic changes or thrombi in veins. It is, however, not reliable for demonstration of the suitability of veins for fistula, since it can not distinguish between thin-walled veins unsuitable for anastomosis and more thick-walled veins. Evaluation of the venous side must mainly be done by palpation and by surgical exploration.

Angiography can also give information about the arterial and venous changes caused by the fistula and the blood flow conditions in the region of the fistula. In larger, well-functioning fistulae, the feeding artery is widened. The blood flow is often directed

towards the fistula in both the central and distal arterial limbs, i.e. the flow in the artery distal to the fistula may become retrograde. Flow in the normal direction through the distal artery indicates small fistula flow and is correlated to less satisfactory function.

Phlebography in normal and fistula cases using venous compression failed to show passage of contrast medium from the superficial to the deep venous system below the level of the elbow. This might be of importance for the lack of development of deep venous hypertension, oedema and nutritional disturbances.

Several types of complications may occur in patients having a traumatic or congenital arteriovenous fistula. Thus strain upon the heart progressing to cardiac failure, local circulatory disturbances with claudication and gangrene, morphological changes of the vessels involved in the fistula, disturbed growth of the extremity and endarteritis with septicaemia have been described. When arteriovenous fistulae are made for therapeutic purpose it is therefore of great importance to be sure that no serious complications are caused by the fistula.

The size and location of the Cimino-Brescia fistula makes it improbable that the heart would be seriously affected by the fistula. Many of the patients have, however, already a strained heart due to anaemia, hypertension, overhydration, atherosclerosis etc. This fact also makes it difficult to use common clinical signs of heart failure such as peripheral oedema, changes in heart size, ECG etc for evaluation of the effect of the fistula.

Studies of cardiac output with open and closed fistula showed in all the patients examined a decrease of cardiac output when the fistula was compressed. This decrease is smaller than that found by some authors (Menno et al. 1967, Klinkmann et al. 1967, Lazorthes 1969), but similar to that reported by Verberckmoes et al. (1967) and Heidland et al. (1967). In eight of ten cases it is smaller than 10% of the cardiac output which means that it is of no clinical significance. Compression of the fistula gives no significant change of central venous pressure. A sudden rise in arterial pressure is rapidly adjusted but the arterial pressure is still somewhat elevated. The pulse rate is somewhat decreased but even this is of short duration. The blood pressure changes could mean that the fistula flow may be somewhat larger than the difference in cardiac output.

The studies made give no indication that the arteriovenous fistula would adversely affect the function of the heart in these patients.

The change in cardiac output after compression of the fistula gives an estimate of the fistula flow. The method is, however, relatively insensitive. It would be of great value to have a simple and accurate method for determination of the fistula flow. Electromagnetic flowmeter can be used for flow determination during operation. However, the probes available to us are too big for accurate measurement from the incision used and the method can not be used for control of the development of fistula flow.

Several authors have reported the use of venous occlusion plethysmography for determination of arteriovenous fistula flow (Hurwich 1969, Herron & Wallace 1971). Initially it was thought that this technique could be used (Lindstedt et al. 1967). Further study of the plethysmographic curves and measurement of the fistula venous pressure during venous occlusion have shown that superficial veins in the forearm are filled within one to two pulse beats and the plethysmogram can not be evaluated. Plethysmography can not be used for determination of fistula flow larger than about 500 ml/minute according to our experiences.

The ultrasonic Doppler principle flowmeter was used by Ram & Bhimani (1971) to study blood flow through arteriovenous fistulae. Exact adjustment of the flowmeter to the artery is necessary and the diameter of the artery must be known. Even in the best hands this technique gives at best a semiquantitative index of blood flow. We have no experience with this technique of fistula flow determination.

Preliminary studies have been made using a dye-dilution technique (Lingårdh et al. 1970) but several technical details such as mixture of dye and the suitable place for blood sampling have not been fully studied. It is possible that this technique might be useful. Otherwise it must be concluded that no technique is yet available for the determination and follow up of blood flow through Cimino-Brescia arteriovenous fistulae.

Serious local circulatory disturbances causing ulcerations or claudication are uncommon even in large congenital or acquired arteriovenous fistulae of many years standing. No clinical signs of local circulatory insufficiency appeared in our patients having Cimino-Brescia fistulae. For study of local circulation, the xenon wash out technique was chosen. The muscula-

ture most likely to be affected by the arteriovenous fistula was thought to be that of the short muscles of the thumb and the ability to increase blood flow by reactive hyperemia would be the best indicator of undisturbed local circulation.

It is important to produce maximal ischaemia to get reproducible curves and this requires good cooperation from the patient. No attempts have been made to standardize the working load as muscle power in both arms is not the same and the fistula was mostly made in the nondominant arm. Many uraemic patients also have muscular atrophy due to uraemic polyneuropathy.

Normal values of blood flow of the thenar musculature after ischaemic work has not been found in the literature. The study has been limited to comparison between sides. Certain variations are present but in all patients considerable reactive hyperaemia could be measured. No significant difference in maximal blood flow could be found between the hand having an arteriovenous fistula and the normal hand. The study thus gave no indication of decreased local circulation to the tissues caused by the arteriovenous fistula.

Congenital arteriovenous fistulae and acquired fistulae appearing before skeletal growth is finished may cause skeletal hypertrophy of the extremity with increase both in length and thickness of the long bones. Causes of this increased skeletal growth are not fully known. The most common theories consider an increased rate of circulation and increased temperature in the growth zone, increased oxygen tension in the venous blood and increased venous pressure (for literature review see Persson 1968). Even if some increase in length of the skeleton of the arm is of less importance than the corresponding changes in the lower extremities, fear of skeletal hypertrophy has been one reason why arteriovenous fistulae for haemodialysis have been avoided in children (Robert & van Zyl 1968). In the three children undergoing haemodialysis with an internal arteriovenous fistula no difference in length or structure of the long bones of the lower arm could be measured between sides. Even if the time of observation is not more than two years this indicates that the Cimino-Brescia fistula could be used even in children without risk of skeletal hypertrophy.

The reason why skeletal changes are not found is not quite clear. The time of observation might be too short. Increased blood flow is present in the extremity having an arteriovenous fistula, mainly limited to the

large arteries and the superficial veins. As angiographic studies could not show blood flow from the superficial to the deep veins it is, however, improbable that increased oxygen tension or increased venous pressure is present in the deep veins, i.e. even the veins draining the growth zone of the long bones.

Morphological changes occur in the artery and vein connected to the Cimino-Brescia fistula in the same pattern as is known in other types of arteriovenous fistulae. The vein is dilated and becomes arterialized, i.e. thick-walled and histologically similar to an artery. Causative factors may be increased blood pressure and turbulence of blood flow. These changes can be noted by inspection and palpation of the veins, by angiography and by microscopic examination of specimens from the veins. These changes make the veins easier to puncture and the thickening of the vessel wall decreases the risk of bleeding after puncture and of accidental detachment of the cannulae during dialysis.

Widening of the artery leading to the fistula is a constant finding in cases of well-functioning Cimino-Brescia fistulae studied by angiography. Histological examination of some specimens made at autopsy show very slight changes from normal arteries. No signs of degeneration of the arterial wall or formation of aneurysms have been noticed. The widening of the artery was noticed as soon as 16 days after creation of a fistula in one patient.

The cause for the arterial dilation is not fully clear. A mechanism similar to the stimulation for development of collateral arteries is probable, in fact the arteriovenous fistula is the most potent stimulator known for the development of collaterals around the fistula region. Collateral circulation, sometimes extensive, from the arteries of the lower arm not connected to the fistula can be demonstrated by angiography.

Mörl (1954) suggested that the first noticeable change after an arteriovenous fistula is opened is vasodilatation caused by metabolites from the ischaemic tissue distal to the fistula. Holman (1937) showed, however, that initially a diminution of the arterial caliber is seen. In the present material the mechanism suggested by Mörl could hardly be of importance since there were no signs of ischaemia. When an arteriovenous fistula is opened peripheral resistance is diminished, increased rate of blood flow in the artery develops and the pulse amplitude is increased. Hughes (1937) suggested that an increased flow rate itself can stimu-

late growth of the vessel by stimulating the cells. Petrovsky & Milonov (1967) created experimental fistulae in the neck of dogs and found decreased circulation through the vasa vasorum of the arterial wall. This was thought to be due to decreased lateral pressure against the vessel wall caused by the increased flow rate. They suggest that decreased nutrition to the vessel wall would lead to degeneration of the artery.

Increased flow rate and increased pulse amplitude close to the fistula may contribute to making the arterial blood flow turbulent. Turbulence of arterial blood flow in the present patients is not proven but probable. The presence of pronounced murmur and palpable thrill are in any case signs of vibration of the arterial wall. Arterial dilation can partly be explained and arterial wall degeneration mainly explained as an effect of material exhaustion caused by vibration of the arterial wall.

Vollmar (1964) showed that the arterial dilation is often irreversible even if an arteriovenous fistula is repaired. Foster (1970) reported a case where arterial changes were reversible when they were not too advanced. It is also a well-known fact that collaterals may regress when an arterial obstruction is reconstructed. Decrease of the caliber of the renal artery is a regular finding in patients with renal diseases leading to destruction of renal parenchyma. It is therefore probable that the arterial changes occurring in patients with Cimino-Brescia fistulae would be at least partly reversible.

Thus, morphological changes develop in the artery and vein connected to the arteriovenous fistula. The changes on the arterial side have not been found to be unfavourable to the patient. Observations concerning the eventual development of arterial aneurysms after many years standing of the fistula are, however, recommended. The changes on the venous side, on the other hand, are favourable to the patient and facilitates the use of the arterialized veins.

Endarteritis or endocarditis leading to septicaemia have not been observed in our patients having Cimino-Brescia fistulae and the diminution of the rate of infectious complications is one of the great advantages of the subcutaneous fistula compared to the Quinton-Scribner shunts. Haematoma at the site of puncture of the arterialized veins has been observed and such a haematoma may become infected and has in one case created an infected pseudoaneurysm communicating with the vein. Many of the patients have

increased bleeding tendency and decreased resistance to infections. The risk of bleeding complications and destruction of the fistula by the haematoma are diminished if the fistula veins are not punctured

too close to the anastomosis. If an infected haematoma develops, intensive long-term antibiotic treatment, eventual operation and even ligation of the vessel must be considered.

CONCLUSIONS

After five years experience of 181 patients with Cimino-Brescia arteriovenous fistulae the following conclusions have been reached.

1) Cimino-Brescia arteriovenous fistulae are well suited for use in hemodialysis and they can give as good dialysis effect as Quinton-Scribner shunts. They have several advantages compared to the external shunts, and are particularly suitable for patients being prepared for kidney transplantation. They can be used in children, over 20 kg body weight.

2) Cimino-Brescia fistulae can be used for injections of drugs, which are usually locally irritating, for taking blood samples, and for intravenous therapy after major surgical operations.

3) It is much easier to create functioning fistulae in patients with uraemia than in patients with normal blood coagulation. Estrogen therapy increases the risk of postoperative thrombosis of the fistula. If a good functional result should be expected, a normal large subcutaneous vein must be available in the lower arm. Veins with postthrombophlebitic changes can be used for creation of a fistula in uraemic patients but not in patients without uraemia. If thrombosis of the fistula occurs, reoperation should be attempted but the results of thrombectomy are poor.

4) Side-to-side anastomosis is fully satisfactory in most patients and other types of anastomosis have not given any advantages. Deviations from the standard surgical technique are indicated only where the construction of a side-to-side anastomosis is technically difficult. If a suitable subcutaneous vein is not available in the lower arm a bridge graft of saphenous vein can be used.

5) The fistula can be used within one week after operation in most cases. It is preferable, however, to create the fistula early since construction of a fistula several months before expected use has no disadvantages.

6) When a patient is scheduled for kidney transplantation an arteriovenous fistula should be created even if the need for hamodialysis is not expected in the near future. The arterialized veins can then be used during the pre- and postoperative periods for taking blood samples and for intravenous therapy, and even-

tually haemodialysis. Otherwise the subcutaneous veins might be destroyed by venous puncture for blood sampling and injections and the later creation of an arteriovenous fistula might be difficult.

7) The Cimino-Brescia fistula gives rise to the well known vascular changes connected to arteriovenous fistulae with widening of the artery and arterialization of the vein. Degeneration of the arterial wall with aneurysm formation has not been seen and no signs of impaired growth or hypertrophy of the extremity have been noted.

8) The Cimino-Brescia fistula is not a handicap for the patient, does not impede daily living and does allow him to perform hard manual labour.

9) Brachial angiography is a simple technique suitable for examination of the vessels in the patients with poor fistula function. It is also suitable for studies of the arterial tree to find an artery for anastomosis but is less satisfactory for studies of the anatomy on the venous side.

10) No signs of impaired local circulation in the fistula extremity have been observed and after local intramuscular injection of radioactive xenon, reactive hyperaemia after ischaemic work can be measured.

11) Determination of cardiac output with open and closed fistula together with measurement of arterial pressure, pulse rate and central venous pressure does not indicate adverse changes of cardiac function in the patients studied.

12) The subcutaneous veins in the lower arm on the fistula side contain arterial blood which can be used for arterial blood gas determination and thus arterial puncture is avoided.

13) Determination of the cardiac output with open and closed fistula gives a rough estimate of the blood flow through the fistula. Fistula flow can not be measured using plethysmographic technique and no ideal method for the determination of fistula flow is available.

14) Infected pseudoaneurysms after puncture of the arterialized veins can give rise to septicemia. Septic infections like endocarditis lenta have been described in the literature but have not been observed in our patients.

SUMMARY

The literature concerning arteriovenous fistulae including their etiology, haemodynamic effects and treatment is reviewed.

The surgical technique for construction of Cimino-Brescia arteriovenous fistulae, mostly side-to-side between the radial artery and the cephalic vein, is described in detail.*

Surgical results in 181 patients operated by the present author during somewhat over five years are reported. In the first group of patients, 103 cases, the fistula was made for haemodialysis. In this group it was possible to create functioning fistulae in all cases.

The second group, 51 cases, had a fistula made to facilitate intravenous injections of a cytostatic drug for the treatment of prostatic carcinoma. In this group 39 (76%) obtained a functioning fistula.

The third group, 27 patients, had generally poor veins and the fistula was created to make long-term intravenous therapy easier or possible. In this group the operation was successful in 17 (63%).

The difference in surgical results is most probably mainly due to changes in the clotting and fibrinolysis mechanisms. The importance of the condition of the vein and the poor results in cases where the main veins were damaged by previous thrombophlebitis are pointed out.

Brachial arteriography was performed in 24 patients, phlebography in two patients with fistula and five healthy controls. Angiography proved to be a good method to study patients with poor fistula function and to study the conditions on the arterial side where a new fistula was planned. Widening of the artery leading to the fistula was found in all cases of good fistula function. Phlebography is useful to show thrombotic changes or occlusions in veins leading from the fistula but is not useful for demonstration of veins suitable for anastomosis. No communications between superficial and deep veins could be demonstrated in

persons without fistulae or in two patients with fistulae.

Haemodynamic studies including determination of cardiac output with open and closed fistula, central venous pressure, heart rate and arterial pressure were performed. On occlusion of the fistula a decrease in cardiac output was found in all the ten patients studied. The mean decrease was $7.6 \pm 6.0\%$. No significant change in central venous pressure was recorded. The arterial pressure was raised on compression of the fistula and the pulse rate decreased. These changes are rapidly adjusted. The blood from the veins draining the fistula was found to have P_{O_2} levels of the same size as the arterial blood.

In thirteen patients ^{133}Xe clearance was measured in the adductor pollicis muscle of the fistula hand compared to the normal hand. No consistent differences in resting flow or maximal blood flow after ischaemic exercise could be found.

It is concluded that no adverse effects upon central or local circulation could be attributed to the Cimino-Brescia fistula.

Of other possible complications to the fistula, changes in the vessels, hypertrophy of the limb, and septicaemia are discussed. Widening of the artery and vein are found regularly. Hypertrophy of the limb was not found in three children. Septicaemia occurred secondary to an infected haematoma after venipuncture but endocarditis or endarteritis were not observed.

Determination of cardiac output with open and closed fistula gives a rough estimate of fistula flow.

It is concluded that the arteriovenous fistula according to Cimino-Brescia is a valuable technique for use in haemodialysis and for intravenous injections. No deleterious effects of the fistula have been found which would preclude its use in appropriate cases. Increased clinical use of the fistula technique is recommended.

*This technique is also described in an audio-visual programme produced by AB GAMBRO^R, Lund, Sweden.

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